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TRANSACTIONS & STUDIES

of the

College of Physicians of Philadelphia

Volume 19 (Fourth Series)

Number 1 (April 1951)

Public Health as a Weapon for National Defense*

By JAMES STEVENS SIMMONS, M.D., Brig. Gen., USA (*Ret.*)

Dean, School of Public Health, Harvard University

I THANK you for asking me to attend this meeting of your distinguished College. I appreciate deeply the honor of being invited to deliver the XXVth James M. Anders Lecture.

It is always pleasant to return to Philadelphia where I was graduated in medicine shortly before we entered the First World War and where I still have many good friends. Naturally I am glad to be here with you and I am pleased with your gracious invitation to discuss an aspect of Preventive Medicine which I consider to be of primary importance to all of us in this grim year of national danger.

Last June when Dr. Hubley R. Owen wrote me about the purposes which Dr. Anders had in mind when he made this fund available in 1924 and of the uses to which it has been put under the direction of your Committee on Public Health and Preventive Medicine, I suggested as a tentative title for my talk, "The Need for Postgraduate Education in Public Health."

Now that our Armed Forces are engaged in a desperate fight against Communism in Korea and our nation is rapidly mobilizing for the even graver task of waging a third global war, I should like to change this subject. Instead I propose that tonight's discussion be called "Public Health as a Weapon for National Defense." I also propose that, as we discuss this subject, all of us give earnest consideration to the possibility of developing without delay a strong, closely knit, all-out national program of medicine and public health, which will be aimed directly at the conservation of the health and strength of the country's most important resource—its fighting and working manpower.

THE NATIONAL EMERGENCY

The year 1950 will stand out as a critical period in our national life. It was a year of increased international tension created by the mounting threat of Communist domination of the free nations of the world. The unprovoked attack on the people of South Korea on June 25 brought into clear focus the challenge faced by the United States and the United Nations. This barbaric attack convinced those, who have been hoping and working for international peace since World War II, that the one serious obstacle to the success of their plans is the Soviet Union. The failure of Communist Russia to cooperate with the United Nations, her

* James M. Anders Lecture XXV, The College of Physicians of Philadelphia, 7 February 1951.

ruthless behavior in the subjugation of satellite countries, and her wide-flung, subversive operations designed to stir up discontent in underdeveloped regions have left no doubt of her malignant intention to dominate the entire world by force, either through destruction or by slavery. The North Korean attack and the subsequent uncivilized action of the Chinese Communists have convinced the people of the United States that they must mobilize their entire strength in order to remove this threat to their survival in a free world.

To meet this challenge successfully, we must develop a strong defense program utilizing our total resources. Such a program will require wise planning geared to whatever the future may bring. We must prepare to meet an immediate attack, followed by an all-out global war. At the same time we must be prepared for a long period of armed defense against a conflict which may or may not be forced upon us. In either case the program will call for great courage and sacrifice and for the conservation of all our resources and strength. The most important resource of the nation is its manpower, and it is with this aspect of the defense program that we are most concerned.

PUBLIC HEALTH AND MANPOWER

The present threat affords a unique opportunity for greater service through public health. There is a direct relationship between health and manpower. This relationship is so obvious that it should require no discussion. Modern public health now has available effective methods which can be used to protect individuals and large aggregations of people against many diseases and to conserve their health and strength.

Public health is simply the wholesale application of community preventive medicine to large groups of individuals. Its purpose is to keep well people well in body, mind and spirit. Evidence of its practical importance is afforded by the improvements in both civilian and military health in the United States during the last five decades. These improvements have resulted in an enormous saving in industrial manpower and a general strengthening of America's human resources. Military preventive medicine, which is really military public health, paid rich dividends in the conservation of America's fighting manpower in the last war. Half a century ago, during the Spanish-American War, the rate for disease deaths among our troops was about 25 per thousand per annum; and 13 American soldiers died of disease to every one killed in battle. During the First World War the rate was reduced to about 16; and the ratio of disease to battle deaths was only one to one. As midcentury approached, public health knowledge and techniques were so improved and so effectively applied that in World War II the disease death rate for our total Army of about 10 million men was only 0.6 per thousand per annum; and in the European Theatre only one soldier died of disease for every 85 killed in battle. This experience of the recent past gives proof of the fact that the profession of public health now has at hand methods which can be used to conserve both civilian and military manpower.

PUBLIC HEALTH AND NATIONAL DEFENSE

It is imperative that a fully effective program of disease prevention be developed as a basic requirement for national defense. Only by the mobilization of our total health resources and the adoption of a nation-wide program of preventive medicine and public health can we hope to accomplish this. Such a program affords a logical approach to the conservation of America's strength in a manner which will enable her people to meet successfully the present threat of war. The nation's leaders must recognize the fact that the health of the American people is the keystone of the nation's strength.

The potentialities of such an all-out preventive program can be visualized by reviewing the present status of American health, and by considering the various factors that have influenced the progress already made. Such a review shows that further action will be required to correct certain existing deficiencies.

There is need for vigorous, intelligent planning on the part of our political leaders; and they must be guided by equally intelligent, united leadership and advice from the best qualified experts in the professions of medicine and public health. Moreover, whatever program is adopted must have the full support of all our citizens.

Granted such united professional and political leadership, America's wartime preventive medicine program can become one of the most powerful weapons available for the nation's defense.

PRESENT STATUS OF THE NATION'S HEALTH

In taking stock of the present status of American health, it should be remembered that public health is a relatively new specialty of the much older profession of medicine; that it has attained professional status only recently, and that most of the great advances made by both these professions have been accomplished within comparatively recent times. Such a perspective will enable one to avoid the mistake of concluding that the progress already made in either of these fields is satisfactory, or that their full potentialities have been realized. Moreover, an objective review of the present situation will make it possible to visualize clearly the present opportunities for strengthening America's total facilities for disease prevention and health conservation.

Civilian Health

Three years ago, a "century of progress in public health" was celebrated in this country. At that time we cited the advances in sanitation, medicine, preventive medicine and public health since 1848, when Lemuel Shattuck was appointed to make a survey that led to his now-famous health report to the Massachusetts Legislature. We traced the slow evolution of the modern profession of public health following Shattuck's early vision of a new type of national service based on research and education, both focused on prevention of disease. As more exact knowledge about the control of disease became available through research, it stimulated an increasing interest in the new specialty of preventive medicine. Eventually, this led to the establishment of formal departments of preventive medicine in certain medical schools, and, later, to the present postgraduate schools or departments of public health. The current military situation makes it of interest to reemphasize the important influence of officers of the Medical Department of the U. S. Army on the evolution of both military and civilian preventive medicine and public health.

The present status of civilian health is much better than it was at the time of the Spanish-American War. The death rate for the United States has decreased from 17 to less than 10 per thousand; and the expectation of life at birth has increased from about 47 years in 1900, to an all-time high of more than 67 years in 1950. The adoption of better preventive measures in obstetrics and pediatrics has caused a decrease in maternal and infant mortality within the last two decades. The communicable diseases of childhood are still prevalent but they no longer cause the high mortality rates of the recent past. Fifty years ago the combined death rate for measles, scarlet fever, whooping cough, diphtheria and meningitis was 75 per 100,000. In 1940 the rate was only 2.5—a reduction of about 97 per cent. Likewise, the morbidity and mortality rates for infectious diseases of the intestinal, respiratory and insect-borne groups have been decreased. In brief, considerable progress has been made in protecting the civil population against disease. The status of civilian health in this country now compares favorably with the level of health in most of the leading nations of the world. Nevertheless, the full potentialities of public health have not yet been realized.

Military Health

The health of the Armed Forces located in this country compares favorably with civilian health. In fact, the peacetime health of troops stationed in permanent posts in the continental United States is better than that of the average non-military citizen. This is true for a number

of reasons. In the first place, the military forces are made up largely of vigorous young adults who have been selected carefully because of their relatively good physical condition. In the second place, the American military man's way of living, including his personal hygiene, diet, housing and physical training is regulated. He is immunized against smallpox, typhoid, tetanus and many other infectious diseases to which he may be exposed. He lives in a carefully sanitated environment which is rigidly controlled by a well-organized medical department, the primary concern of which is to protect him against disease and to maintain his total health in order to keep him fit to fight.

The hardships imposed by field service and combat make it difficult to maintain this type of health protection under war conditions. Therefore, in our present plans to strengthen the nation's health program for defense, primary consideration must be given to protecting the Armed Forces against the unusual disease hazards of war. Because of their recent experience in World War II, the medical departments of the Army, Navy, and Air Force are now in a strategic position to expand their preventive medicine programs as rapidly as may be required to meet the threat of a third global war.

Military leaders now recognize the fact that a strong program of military preventive medicine is a basic requirement for the successful conduct of modern war. It is the responsibility of the Medical Departments of our Army, Navy and Air Force to protect the health of the soldier, sailor and airman in a manner which will maintain at all times his physical and mental effectiveness as a fighting man. This requires first aid in battle, rapid evacuation of the wounded and the provision of modern treatment and medical care for the sick and wounded; but an even more important requirement for the fulfillment of the Medical Department's responsibility is through the prevention of disease and disability. Therefore medical officers of the Armed Forces have always been interested in the development of preventive medicine and they have contributed much to its advancement.

This interest was born of bitter experience; for prior to the present century, all our wars were fought without benefit of preventive medicine. In the numerous Colonial Wars and in every conflict from the American Revolution to the surrender of Lee at Appomattox, there was always the threat that our troops might be defeated by disease. In each of these early wars there was an enormous waste of manpower through sickness and death caused by the uncontrollable infectious diseases. When the researches of the latter half of the 19th century began to produce exact information about the microbiological causes of disease, the Army medical officer naturally was among the first to apply this information to his difficult wartime task of protecting the health of troops.

Early Improvements in Military Health

It is fortunate that, during the so-called "golden age of medical discoveries" which followed the Civil War, the U. S. Army had as its Surgeon General Dr. George M. Sternberg, who was a scientific investigator and a national medical leader of great vision. During his early service in the Civil War, General Sternberg witnessed the crippling effects of dysentery, malaria, and the other diseases which ravaged the troops of both Union and Confederate armies. This experience and the subsequent discoveries of Pasteur, Koch, Lister and their followers led him to undertake his pioneer studies in the newly emerging sciences of bacteriology and protozoology. He published the first American textbook on bacteriology in 1884 and was later referred to by the great Robert Koch as "the father of American bacteriology."

Sternberg served as Surgeon General from 1893 to 1902 and during this period he initiated an extensive program of research in military preventive medicine throughout the Army. Following the bitter experience of our troops with typhoid, dysentery and yellow fever during the Spanish-American War, he organized special Army research boards for the study of

diseases in our newly acquired tropical possessions. His broad vision made possible the important researches of Major Walter Reed on yellow fever in Cuba—researches which influenced the later work of General Gorgas on sanitation in Panama. It led to Colonel Bailey K. Ashford's studies which showed that malignant Puerto Rican anemia was caused by massive hookworm infection. It provided for the investigations of Colonel Richard P. Strong on dysentery, plague, cholera and other tropical diseases in Manila and the researches of Colonel Charles F. Craig on malaria in the Philippines and elsewhere, and for the work of Colonel Joseph F. Siler and others on dengue fever. It undoubtedly influenced the later work of General Carl Darnall who gave us improved methods for the chlorination of city water supplies, and the researches of General Frederick F. Russell who developed the triple typhoid vaccine which has been used successfully by the Armed Forces in two world wars. Sternberg's broad concept of the importance of preventive medicine had an influence on all of these contributions, and stimulated other workers of the Army and Navy to conduct researches along similar lines, which have added much to the development of both military and civilian preventive medicine.

As evidence of General Sternberg's leading role in the country's medical and health activities of his time, it is noteworthy that he served as President of the American Medical Association and as President of the American Public Health Association. He was also a pioneer educator in the new field of military and civilian preventive medicine. When he was made Surgeon General in 1893, one of his first acts was to organize the Army Medical School in Washington to provide facilities for research and for postgraduate education of medical officers with special emphasis on prevention. It was not until 16 years later that the first formal department of preventive medicine was established in a civilian medical school. This was done at Harvard University in 1909. Four years later, in 1913, the first postgraduate school of public health was organized in Boston and called the Harvard-Massachusetts Institute of Technology School of Public Health. In 1921 this became the Harvard School of Public Health.

Military Health in the Twentieth Century

Since 1900 the progressive improvement in military health has paralleled closely the advances in civilian medicine and public health. During World War I, both the Army and Navy had good programs of preventive medicine and their health records were much better than in previous wars. Typhoid fever, which had been a serious handicap even as late as the Spanish-American War was well controlled. The most important causes of sickness and death were pandemic influenza and other respiratory diseases. There was little exposure to tropical diseases.

In World War II the health records of the Army, Navy and Air Force showed still further advances. This was due in part to improvements in civil medicine and health following 1919, but largely to the comprehensive wartime program of research which was in operation from 1940 through 1945. Each of the three services developed strong programs of preventive medicine, the effectiveness of which is shown by the statistical results which I cited a few minutes ago. Since 1946 the postwar health of the Armed Forces has been excellent, both in this country and abroad. Striking examples of the improvements made during World War II for the protection of the health of our fighting men are indicated by two incidents that have arisen in the present Korean war. Several months ago a national radio commentator made an erroneous announcement that yellow fever was present in Korea. If true, this might have created a serious situation for the enemy, but not for American troops, since it is the policy to protect our troops against yellow fever with vaccination. Also, according to a newspaper announcement six days ago, epidemic typhus is raging among the Communist forces in Korea. However, this

is no cause for alarm because American troops are protected against this ancient wartime disease by modern methods of vaccination and by delousing with DDT.

In brief, available evidence shows that truly remarkable advances have been made in both civilian and military health during the last century. It also indicates that within the relatively short span of three generations the ancient profession of medicine has given birth to a vigorous new offspring—preventive medicine, and that this young specialty has developed into the useful profession of public health. This profession now has new techniques and methods which can be used to bring about further improvements in military and civilian health. Therefore, it is of vital importance in the present emergency.

AMERICA'S UNSOLVED HEALTH PROBLEMS

The official records also show that there is still much room for improvement in American health, and it is important that this fact be recognized by those who are responsible for building up the nation's program of defense. An examination of current national and state health statistics reveals a number of unsolved problems. The latest records available, which are for 1949, show that large numbers of Americans are still being incapacitated by diseases and accidents—many of which are preventable.

Infectious Diseases

It appears that there is some misunderstanding concerning the present incidence of infectious diseases in the United States. This is indicated by the fact that even professional men sometimes refer to the "conquest" of disease as a thing which has been accomplished. The following quotation from the inaugural address made by the President of the American Medical Association on June 27, 1950, is an example:

> "Dread diseases like typhoid, diphtheria and smallpox—which 50 years ago took a heavy toll in sickness and death—virtually have been eliminated as national health problems, and all the infectious diseases have been brought under effective methods of prevention, control, and treatment."

This statement is so obviously incorrect that it deserves comment only because it comes from an official authorized to speak for the leading medical organization of the country. Because of its publication in the *Journal of the American Medical Association* (July 1, 1950) it might be misleading to some of the distinguished laymen who are planning for the nation's defense.

The real truth of the matter is that there are still numerous infectious diseases that have not been brought under "effective methods of prevention, control, or treatment." Last year, for example, the practicing physicians of the United States certified that there were more than two and one-half million infectious diseases in the group of so-called "reportable" communicable diseases. Many of these infections, as for example poliomyelitis and even measles, have not been brought under effective methods of prevention. In addition to this large group of reportable diseases, there were many millions of other infections which are not reportable. The common cold, for example, has not been controlled. Each year it causes suffering and reduced efficiency for about one and one-half billion days. The annual national cost of the common cold alone has been estimated at more than four hundred million dollars; and, when the expense for drugs and medical care are added, the estimated total is about one billion dollars a year. Obviously, the infectious diseases are still a serious handicap to American effectiveness and they still cause an enormous loss in manpower.

Last year more than a million and one-half childhood infections were reported. Also, there were about half a million infections of the respiratory tract, 74,000 intestinal diseases, 6,790 insect-borne infections, and one-half million venereal infections. It is significant to add that methods are now available for the prevention of all these venereal and insect-borne diseases and for many of the filth-borne intestinal infections.

These facts prove that the American people are not yet deriving the full benefit of our present-day knowledge about the prevention of disease and that we have a long way to go before we dare announce that the infectious diseases are really under control.

Accidents

There are other major health problems that demand attention. For example, the reports of the National Safety Council show that in 1948 a total of more than 10 million Americans were injured and 98,000 were killed by accidents. The annual economic loss caused by accidents was estimated to be more than seven billion dollars. When the number of working years lost through premature accidental deaths is added to the actual cost of these deaths, accidents rank as one of the most serious health problems of the country. Their prevention is important to the defense health program.

Mental Diseases

Mental diseases constitute a serious health problem, for which adequate preventive measures have not yet been developed. According to Menninger (1948) one-fourth of the patients in our general hospitals are there because of emotional reactions. A large proportion of the nation's expensive hospitalization is used for mental patients. Almost 300,000 Americans are admitted to mental hospitals every year; and about three million children have emotional or behavior disorders. Any comprehensive program for national preventive medicine must include adequate research aimed at the prevention of diseases of the mind. It seems possible that many of these mental diseases may represent the late and therefore inapparent results of injuries to the nervous system caused by certain of the still-abundant infectious diseases. This is a lead that should be investigated.

Degenerative Diseases

Another unsolved health problem is presented by the chronic degenerative diseases which are now the leading causes of death. An analysis of 1,446,000 death certificates filed in 1949 shows that 746,825 of these deaths were attributed to cardiovascular-renal diseases; that 210,896 were caused by cancer and other neoplasms, and 24,488 by diabetes. These same figures indicate that about one-half of all the people who died in 1949 were 65 years of age or older. This emphasizes the need for basic research to discover methods for the prevention of cancer and the chronic degenerative diseases. They also point up the need for better methods of rehabilitation. It should be possible to salvage much manpower for defense from that large segment of the population which is now wasted because of death and the disabilities of disease, accidents and old age.

Other Health Problems

These are only a few of America's current health problems. Others include the unnecessary loss in working manpower caused by uncontrolled occupational and industrial hazards and diseases. There are also the serious problems of nutritional deficiencies, poor housing, atmospheric contamination, pollution of our streams with sewage and industrial wastes, and the need to conserve and protect our national water supplies. In the field of Maternal and Child Health alone, which is so important in terms of manpower in the next generation, there is much room for improvement. This was shown by the large number of physical and mental defects found in young men examined by the draft boards in the last war. To meet President Truman's peacetime goal of 3,500,000 men for the Armed Forces will require the drafting of more than 1,000,000 men each year. Since last June, a million of these young men have been examined and rejected as physically, mentally or morally unfit. While these figures for rejected draftees are influenced by the changing physical standards adopted from time to time by the Armed Forces and while some of the physical and mental defects listed in this long catalog of persons unfit for service are minor, the fact remains that this nation-wide survey of the physical and mental stamina of our youth

indicates that we have not yet made the most of our health facilities.

New Wartime Health Hazards

In addition to these unsolved peacetime problems, we must also consider the new disease hazards of a modern war, which might easily begin with an atomic attack on the United States and require the simultaneous use of American troops both in this country and abroad. This means that the civil population must be prepared for the occurrence of unusual diseases which might accompany such disasters as sabotage or bombing or those produced by atomic, biological or psychological warfare. It also means that civil health agencies must be prepared to combat an infinite variety of diseases and epidemics, many of which are now considered under control. The Armed Forces must be ready to face these same new hazards. In addition they must be prepared to meet the wartime diseases which they will encounter in military operations at home or abroad.

MOBILIZATION OF PUBLIC HEALTH FOR THE NATIONAL EMERGENCY

The existence of so many unsolved health problems at this late date in our national development is disappointing. It shows that while we boast about health the American people still do not have adequate health protection, and that the nation still is not utilizing its total resources for the prevention of disease. If we are to provide and maintain the healthy manpower required in the present emergency and for the infinitely greater demands of a long war, we must organize a stronger health program with primary emphasis on the prevention of disease.

The defense health program must provide for both curative and preventive medicine. Curative medicine and medical care are necessary to restore to health the sick and injured; preventive medicine is essential if we are to keep more well people well. It is logical, even in peacetime, to place the greater emphasis on preventive medicine in order to decrease expensive hospitalization and medical care. In time of war there is the added need to keep well people well because the entire population is needed for active duty either on the home front or in the fighting lines.

The Preventive Attitude

If the country is to make the most of its latent preventive facilities, a number of important changes must be made. The first, and to my mind the most necessary of these, is to re-emphasize the importance of preventive medicine. Every member of the professions of medicine and public health should make it his business to know what needs to be done to prevent disease in this country, and regardless of his primary specialty, he should work unselfishly for the accomplishment of this objective. If all our 200,000 physicians will apply the principles of preventive medicine to the families of their patients, and give enthusiastic support to their community health programs; if all the country's hospitals will accept the added responsibility of serving as real health centers for their communities with a view to keeping the people well; and if sufficient health agencies manned by adequate numbers of competent specialists are provided for the entire country, the physical, mental and moral fiber of the nation can be enormously strengthened.

This is not just a Utopian dream; but to accomplish it quickly is admittedly a difficult task which will require many revolutionary changes. One basic need is for a thorough revamping of the curricula of the 79 medical schools in order to give the medical graduate a better concept of the practical importance of preventive medicine and public health. He should be indoctrinated with the preventive attitude. This will help to prepare him for his wartime responsibilities either in civil defense or in the Armed Forces. It should also assist in recruiting the health specialists now urgently needed to man our official and non-official civilian health agencies and for the preventive medicine organizations of the Army, Navy and Air Force.

Need for More Health Services and Personnel

The development of a civilian health program for the emergency will require the early correction of certain basic deficiencies. At present there are not enough health specialists to staff properly the existing state and local health departments. This shortage in trained personnel recently has assumed greater importance because the health commissioners of states and many of the directors of local health departments are now charged with important additional responsibilities and services in connection with civil defense.

Another deficiency that must be corrected is the inadequate coverage of the United States by local health departments. Several bills intended to provide for such coverage by local health units have been considered by the Congress during the last few years, but so far they have met with medical opposition and defeat. Local health units are necessary for civil defense and the time has come for positive action which will provide them.

Likewise, the development of an emergency health program for the Armed Forces will require careful planning geared to meet the peculiar circumstances of the present Communist threat. It will be necessary for the Army, Navy and Air Force to develop firm mobilization plans for the rapid expansion and reactivation of their programs of preventive medicine along the lines developed during World War II. This means that the Secretary of Defense and his newly established Armed Forces Medical Policy Committee (which includes the Medical Director of the Department of Defense, the three Surgeons General, and three civilians) are responsible for a difficult task.

To expand the present preventive medicine programs of the three armed services sufficiently to meet the additional requirements of our forces now fighting in Korea, for the national mobilization and training activities now under way, and for the still greater needs of another global war will call for large numbers of experts trained in every aspect of public health. Certain parts of this training can be provided within the respective services; but large numbers of the officers needed for key positions will require postgraduate training of the type now available only in the country's ten accredited postgraduate schools of public health. It takes time to carry out such training, and each of the services should rapidly develop adequate pools of specialists to meet their entire needs.

During the last war both military and civil health were handicapped because it was necessary for the Armed Forces to draw such personnel largely from the inadequate group of trained specialists required by the civil population. This weakened to a dangerous degree the staffs of civilian health agencies and the faculties of schools of medicine and public health. In the present emergency, this mistake must not be repeated for to do so would be like destroying the goose that laid the golden egg. Recent advances in military aviation have increased the chance of air attacks on American cities. This threat of civil disaster and the need to prepare for a long period of armed defense make it essential that adequate personnel also be maintained for the civil health program.

Large numbers of health specialists must therefore be mobilized and the supply must be maintained in order to operate the nation's wartime military and civilian health programs. The President and his Cabinet now face the important question as to how these experts are to be provided.

The Shortage of Trained Health Specialists

The personnel required for this purpose includes large numbers of health workers trained in a variety of specialties, including: health administrators, epidemiologists, public health laboratory experts, public health nurses, health educators, biostatisticians, nutritionists, industrial and sanitary engineers. For the key administrative and professional positions, there is urgent need for physicians with the additional postgraduate training required by the recently established American Medical Asso-

ciation Board for the certification of specialists in preventive medicine and public health. This is available only in the ten Schools of Public Health.

There has always been a shortage in such specialists and with the recent demand for better health facilities, this shortage has become critical. Many state health departments now have unfilled vacancies and the deans of the schools of public health are unable to find applicants for the numerous positions brought to their attention. Two years ago the Commissioner of Health in New York City reported vacancies in that department representing a total salary allotment of about one million dollars. Recently, at the request of the Association of Schools of Public Health, a survey was made by experts of the Public Health Service to determine the needs for the various types of public health specialists required to operate the nation's civilian peacetime health program. These estimates were tentative and may require adjustment. However, they indicated that the projected annual need for personnel with postgraduate training of the type given in schools of public health is about five times greater than their present output.

Need for Recruitment and Training of Health Specialists

Because of the need to expand both the civilian and the military health programs, immediate action must be taken to correct this unfortunate shortage of personnel. Otherwise the country will be handicapped by another example of "too little and too late."

To meet the personnel needs, two things are necessary. The first is to make firm arrangements, which will prevent waste of the trained health specialists now available. Every health expert in the country should be made available throughout the emergency for the work for which he is trained and qualified. The second is to make equally firm plans to recruit the additional health specialists needed and to provide adequate facilities for their specialized training.

The problem of recruitment has been considered for some time by various professional groups and agencies with indifferent success. An active program is now required. To be effective, the emergency recruitment program will require the full backing of the medical profession and much greater emphasis on the importance of preventive medicine in the curricula of the medical schools.

Emergency Expansion of Training Facilities

The problem of the emergency expansion of our facilities for postgraduate training also demands attention. Most of the ten American schools of public health, like the 79 medical schools, do not have adequate funds with which to meet their peacetime obligations. This applies especially to schools which are not supported by state funds, but have been financed in the past largely through gifts from philanthropic individuals or organizations. Such sources are no longer providing sufficient support and many schools are now operating precariously on inadequate endowment income supplemented by temporary "project" grants, most of which come from government agencies.

The existence of this unfortunate financial dilemma in our schools of public health and medicine has naturally been a matter of grave concern to the deans of these schools and to the presidents of their respective universities for a long time. It has been obvious that the operation of an activity so basic to the nation's welfare should not depend for its support on the unpredictable whims of charitable donors. Therefore, most of the deans who are responsible for the operation of our professional schools have felt that the Federal Government should provide at least a portion of the funds required to stabilize their operations. With this thought in mind, officials of the Association of Schools of Public Health and of the Association of American Medical Colleges, within the last few years, have helped to prepare and have sponsored a series of congressional bills designed to accomplish this and to

stabilize the operations of the nation's schools of public health, medicine, dentistry, nursing, and certain other specialties.

Last year a bill providing federal aid to medical and health education was passed by a unanimous, rising vote in the Senate. Its counterpart was opposed by the American Medical Association and was never reported out of the Interstate and Foreign Commerce Committee of the House. The AMA has recently announced the formation of a Medical Education Fund through which it hopes to obtain voluntary contributions, largely through physicians, for the financing of medical schools. Any assistance provided from this source will, of course, be helpful. However, it is completely unrealistic to believe that this plan will meet the operating deficiencies of the medical schools or the emergency need for increased professional training in medicine. Moreover, it does not provide for contributions to schools of public health.

Clearly, the emergency will require partial support for education in medicine and public health either by congressional appropriation or by executive allocation of funds that have been or may be placed at the disposal of the Federal government for use in national defense. At this time when billions of dollars are being committed to armaments, to civil defense, to international propaganda and to assistance for other free nations of the world, it is equally urgent that this country invest as much capital as may be necessary to conserve the most important resource of all—American manpower.

Political and Professional Obstacles to Health

One of the most serious obstacles to the development of an adequate health program in the recent past has been disagreement among representatives of leading professional organizations as to what kind of national program the country should have and who should operate it. Bitter controversies which have arisen out of this difference of opinion have been confusing, both to the layman and to our political leaders. In fact, public health has become a political football.

The viewpoint of the man in the street is simple and direct. He wants to be assured that, if he or his family become sick or disabled, they will receive the best medical care possible and that he will be able to pay for it. He is bewildered at times by the frequent misuse of the term "health" and by loose statements which seem to imply that the provision of hospital facilities, medical care and insurance might cover his total health needs. He would prefer some type of protection which would keep him and his family from getting sick and in this way reduce for them the ever present hazard of suffering and expense. He has heard so much about the manner in which preventive medicine helped to keep American troops in good fighting trim during World War II that he naturally expects to see these same principles applied to his family and his community.

This logical thinking on the part of the layman has been reflected in the extraordinary interest which our lawmakers have shown in public health. Within the short period since World War II, hundreds of bills intended to improve various aspects of medicine, dentistry and public health have been presented and considered by our federal and state legislative bodies. Many of these bills were poorly conceived and have failed, deservedly, because their proposals were founded on poor professional advice. Others, written with the assistance of outstanding specialists in medicine or public health have also failed because of disagreement within the ranks of these professions. A well-known example of this disagreement is afforded by the present fight over "socialized medicine" and "compulsory health insurance," neither of which appears to be desirable or popular. It appears that the energy and funds now being used to battle the fancied dangers of medical socialism might be spent more profitably against the very real dangers of Russian Communism. The most urgent requirement is united, authoritative, professional

leadership. This is needed to assist the President, the Congress, and those who are responsible for planning the defense program.

New Channels for Leadership

In 1947 at the Annual Convocation of the American College of Physicians in San Francisco, I proposed a plan which could help in the development of such united leadership. At that time I recommended:

> That a permanent national advisory and planning council on health be organized with broad, official representation, including members elected from the American College of Physicians, the American College of Surgeons, the American Medical Association, the American Public Health Association, and all the other leading organizations competent to deal with medicine and public health. Such a representative council could concern itself with long-term planning for: (1) the improvement of teaching in medicine and public health; (2) the stimulation of medical research; and (3) the development of a sound program for the education of the public in the principles of health. In addition, this council could act in an advisory capacity to the government in all matters of health legislation.

Two years later, action was taken by another professional group, which is in conformity with this recommendation. In 1949, there was established in the City of New York an organization known as the Inter-Association Committee on Health. The appointed members of this Committee consist of three individuals from each of the following six organizations: The American Medical Association, the American Dental Association, the American Nurses Association, the American Hospital Association, the American Public Health Association, and the American Public Welfare Association. In each instance, membership is restricted to officers of the constituent associations or to members who have important policy-making responsibilities. The primary objective adopted by the Inter-Association Committee on Health is stated as follows: "to study and discuss various phases of health care in the interest of improving the health of the nation".

The existence of this new body brings together officials from the major professional associations in the fields of medicine and public health. It makes available a potentially useful agency which can assist the government in making sound emergency health plans. The members of this Committee share with our statesmen and political leaders a grave responsibility in this time of peril.

Emergency Department of Health

The difficult problem of how to develop an emergency health program now confronts the President, his cabinet, and the staff of special assistants to whom he has delegated the responsibilities of mobilization. The answer to this problem must be found quickly, because the success of their plans will depend on the level to which the health of the entire population can be raised and maintained and the time required to bring this about.

It would, therefore, seem wise to set up at once an emergency federal Department of Health with cabinet status, headed by a Secretary of Health, who is a physician trained in public health and whose abilities and vision are recognized by real leaders of the professions of medicine and public health. This department could be similar to the one proposed on February 19, 1949, in the American Medical Association's twelve-point program for improving national health. The Secretary of Health would be responsible for the coordination and integration of all federal health activities, except those of the Armed Forces. I believe that a strong federal department of public health would facilitate the rapid mobilization of America's health resources to meet the present emergency. Its establishment at cabinet level should provide for close cooperation with the Secretary of Defense and his medical staff. Thus it would be possible to develop a closely integrated national program to conserve the health of both the civil population and the Armed Forces.

The broad objectives of such an integrated emergency program should be aimed at

meeting two basic needs. The first of these is for better application of all the curative and preventive knowledge now at hand. The second is for a more vigorous program of national research aimed at the early discovery of better methods for the prevention of disease and the conservation of health.

From the experience of a lifetime spent in fields of military preventive medicine and civil public health, I am convinced of the fundamental soundness of these objectives. I am also sure that this country is amply endowed with both the facilities and the professional talent required to organize a fully effective emergency health program based on these objectives. At the same time recent experience with various agencies concerned with national planning has also convinced me that these objectives cannot be attained quickly or effectively unless some individual or group is given the primary responsibility and authority to direct the planning and execution of the emergency civil health program.

This statement is no reflection on the competence of the various officials now concerned with different aspects of the national health program. No one of these individuals now has sufficient authority to give this program the force and leadership which it requires. It is only logical to expect that their present divided responsibility and authority interfere with the swift achievement of effective results which are now so urgently needed.

The President has vested Mobilization Director Wilson with vast power. As Secretary of Defense, General Marshall, through his Medical Director, has been given full authority in the field of military health. Thus a sound and necessary principle of efficiency is being applied in government during the national emergency. I believe that this same principle of central responsibility and authority should also be applied at this time to the tremendous task of conserving our civil public health. In this way I am confident that the nation can attain the full measure of human strength which is demanded for the crucial years ahead.

In conclusion I should like to express the hope that this distinguished body, the College of Physicians of Philadelphia, will exert its full influence to bring about the development of the type of defense health program which I have proposed tonight. It has been a long time since a former president of the College recommended the firing of all the guns in the city of Philadelphia in an attempt to stop the devastating yellow fever epidemic which occurred here in 1793. Since that time your membership has included large numbers of the nation's leaders, who have contributed much not only to medicine but also to public health. One of your most highly esteemed members, Sir William Osler, years ago made the wise prediction that preventive medicine is the medicine of the future. I can think of no more appropriate time for us all to work for the fulfillment of Osler's prediction than in the present emergency.

The Role of Hepatorenal Vasoactive Factors in Experimental Shock, and in Experimental Renal and Human Essential Hypertension*†

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IT IS now somewhat over five years since the studies were initiated in our laboratory which the College of Physicians of Philadelphia has so signally honored by its bestowal of the Alvarenga Prize Award. I want to express, for my laboratory, our deeply felt appreciation that this distinguished body should have felt that our studies merited this recognition. In accepting this distinction, I do so as merely the senior member of a group of investigators, representing a variety of disciplines and experimental backgrounds, who have joined with me in what has been for us a thrilling scientific adventure. What has been accomplished is due to the individual, as well as joint contributions of the members of this group, and I wish to take this occasion to express my indebtedness to them: to Dr. Benjamin W. Zweifach, for his fundamental contributions to our present knowledge of the function of the capillary bed in health and disease; to Dr. Abraham Mazur, for the skill with which he has resolved so many of the knotty chemical problems which confronted us; to Dr. Silvio Baez, for his skill in devising and applying experimental surgical procedures; and to Dr. Robert F. Furchgott, for his aid in unraveling the complex metabolic characteristics of the humoral systems with which we have been concerned.

Our studies have dealt with two hitherto undescribed physiological principles, with opposite actions on the terminal vascular bed of such a character as to suggest that they constitute a homeostatic system concerned with the regulation of the peripheral circulation. What I propose to present for your consideration this evening is some of the evidence which we have accumulated as to the modes of origin of these humoral principles, their effects upon the peripheral vascular bed, and the derangements in these mechanisms which suggest that they play an important and possibly critical role in circulatory shock and hypertension.

Inasmuch as our initial studies dealt with circulatory shock, it might be appropriate to begin with this problem. When these studies were inaugurated, the concepts of shock then current failed to provide an adequate explanation for many of the phenomena of both clinical and experimental shock. It was the consensus that the ultimate collapse of the organism was the consequence of peripheral circulatory failure. It was also appreciated that a differentiation must be made between the factors which initiate and those which perpetuate the shock syndrome. Among the factors considered to be involved were fluid loss, neurogenic influences, changes in capillary permeability and toxic humoral agents. However, the relative importance of these factors and their specific influence in different states of shock remained unclear. The earlier postulate by Cannon and co-workers, that deleterious principles resulting from tissue damage initiated the syndrome of traumatic shock and contributed to the fatal outcome, had fallen into disfavor. There was no clearcut evidence implicating specific toxic factors and direct proof was furnished by Bla-

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lock and co-workers that the initiation of the syndrome was, in large measure, attributable to a reduction in blood volume, secondary to the extravascular loss of fluid in the traumatized limb.

However, although the fluid loss concept *per se* seemed adequate to explain the initiation and the early manifestations of the shock syndrome, such as hypotension and vasoconstriction, it threw no light on either the nature of the compensatory mechanisms involved or the reasons for their deterioration as the shock syndrome progressed. The latter phenomenon is of particular importance in relation to the development of increasing refractoriness to fluid replacement therapy and eventual irreversibility, a condition which occurs not only in clinical shock but which can be regularly produced in animals by standard experimental procedures. Furthermore, no explanation was provided for death from tourniquet shock of animals whose limbs were tightly taped to prevent significant fluid loss.

The direction of our studies was set by the observation of Zweifach, Chambers and their associates, using the vascular reactions of the exteriorized omentum or mesentery as an index, that the shock syndrome in anesthetized animals, subjected to prolonged hemorrhagic hypotension, proceeds in two stages: an initial vascular compensatory and a subsequent decompensatory stage. Before describing the experimental development of this concept in our laboratory, it will be profitable to give some consideration to the architecture, the functional characteristics and the humoral factors which regulate the behavior of the peripheral bed.

Prior to the fundamental contribution of Zweifach and Chambers to our knowledge of the structure and behavior of the capillary bed, this vascular unit was thought to be composed of inert endothelial vessels which served merely for the passive transfer of blood from artery to vein and took no active part in this process. These investigators, however, have clearly shown that the capillary bed, in tissues such as the mesentery, skin, and muscle, consists of a number of distinct structural units. Certain of these vascular units have contractile properties and other functional characteristics by virtue of which they exert a profound and direct influence on the exchange of fluid between the blood and the extravascular spaces. There is, furthermore, a high degree of integration between the activity of the capillary bed and that of the terminal arterioles which are more directly and acutely concerned with the regulation of blood pressure. Hence, changes within the capillary bed are accompanied by readjustments in the arterioles proximal to it and, conversely, constriction and dilatation of the terminal arterioles elicit appropriate responses in the capillary bed. Such an integration is obviously essential to achieve the homeostatic goal for which the circulation is fundamentally designed, namely, the maintenance of a constant cellular environment.

The architecture of the capillary bed as revealed by the studies of Zweifach and Chambers is presented in diagrammatic form in *Figure 1*. The terminal arteriole gives rise to a central preferential or thoroughfare channel, the metarteriole. This vessel is surrounded by smooth muscle cells for a considerable portion of its length and represents the most direct route from the arterial to the venous circulation. It gives off numerous muscular offshoots, the precapillary sphincters which, because of their strategic location, directly control the flow of blood entering the so-called "true" capillaries. The latter arise from the precapillary sphincters and are non-contractile endothelial vessels which eventually merge with one another to form the collecting venules into which the metarterioles also empty their blood.

These muscular units of the capillary bed exhibit a periodic activity termed vasomotion, characterized by alternating periods of constriction and dilatation. They also manifest variations in reactivity which can be recognized by alterations in the sensitivity of their constrictor response to the topical application of epinephrine. Another feature which distinguishes this portion of the vascular tree from the

larger blood vessels is its extreme sensitivity to blood-borne factors. Indeed, the behavior of the capillary bed appears to be exclusively regulated by humoral principles of local or systemic origin without the direct participation of the sympathetic nervous sytem which controls the larger blood vessels. As a result of these properties, several distinct phases of capillary behavior can be differentiated, depending upon the state of activity of the tissue and the nature of the predominating humoral factor. These are given in diagrammatic form in *Figure 2*. In the normal resting state, there is an intermittent opening and closing of the precapillary sphincters, blood flowing now through one, now through another endothelial capillary. When predominance of the constrictor phase of vasomotion exists, there is capillary ischemia, the blood flow being confined to preferential channels as a result of generalized precapillary sphincteric constriction. The third figure in the diagram is illustrative of the hyperemic capillary bed which results from the suppression of vasomotion and the accentuation of the dilator phase of the precapillary sphincters. This circumstance is characterized by an overall blood flow through the entire capillary bed. The consequence of each of these situations for fluid exchange between the capillaries and the tissue spaces is illustrated in

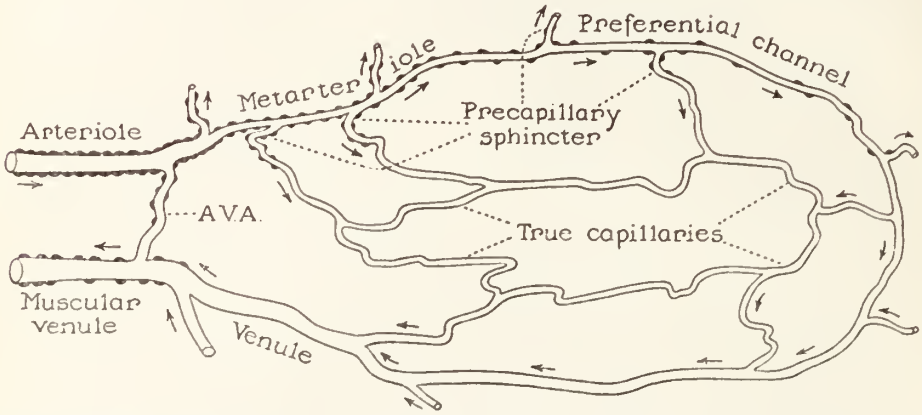

FIG. 1. A schematic representation of the structural pattern of the capillary bed. The distribution of smooth muscle is indicated in the vessel wall.

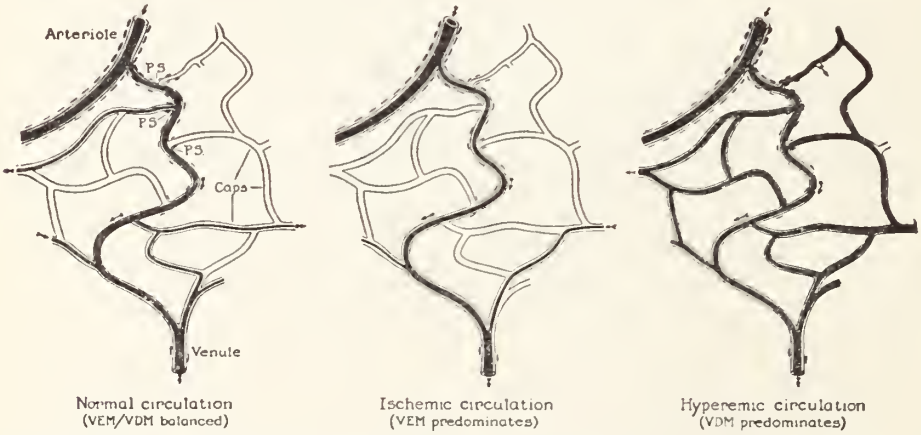

FIG. 2. Diagrammatic representation of the circulation in the terminal vascular bed in the normal, ischemic and hyperemic state. P.S. = precapillary sphincters; Caps. = true capillaries.

Figure 3. The normal pattern of the peripheral circulation is that which serves to preserve a state of fluid equilibrium as seen in resting tissue. During the hyperreactive state, when the constrictor phase predominates in the precapillary sphincters, the number of capillaries through which blood is actively flowing is reduced; and the hydrostatic pressure within the capillaries is diminished relative to the osmotic pressure because of the resistance imposed by the contracted sphincters. The resultant predominance of osmotic forces favors inward filtration, hemodilution and tissue dehydration. The reverse situation is seen during the hyporeactive phase, during which there is an overall capillary flow because of generalized sphincteric dilatation. Hydrostatic pressure can now exert its predominance over osmotic pressure in a larger area of the capillary bed; outward filtration, hemoconcentration and edema formation are favored by this situation.

It is evident that whenever either capillary ischemia or hyperemia are brought about by local or systemic humoral factors, a breakdown of homeostasis would occur unless appropriate compensatory readjustments took place in the arterioles proximal to the capillary bed. As I will point out later in considering the vascular changes in experimental shock and in hypertension, characteristic changes do occur in the capillary bed under these conditions. These changes and the adjustments, or failure to adjust, to them are believed to be of great significance for the reaction of the organism to systemic circulatory alterations.

We may now turn to the humoral factors which are concerned with the regulation of capillary behavior. These vasoactive principles were originally detected by a bioassay method, developed by Zweifach and Chambers, based on microscopic observation of the exteriorized mesenteric capillary bed of the anesthetized rat. This test involves the measurement of the reactivity of the muscular components of the precapillary sphincters, utilizing as an index the constrictor response to the topical application of epinephrine. After determining the threshold concentration of epinephrine to which the precapillary sphincters respond by perceptible constriction and pronounced slowing of the blood flow through the corresponding capillary, the test sample is injected into the

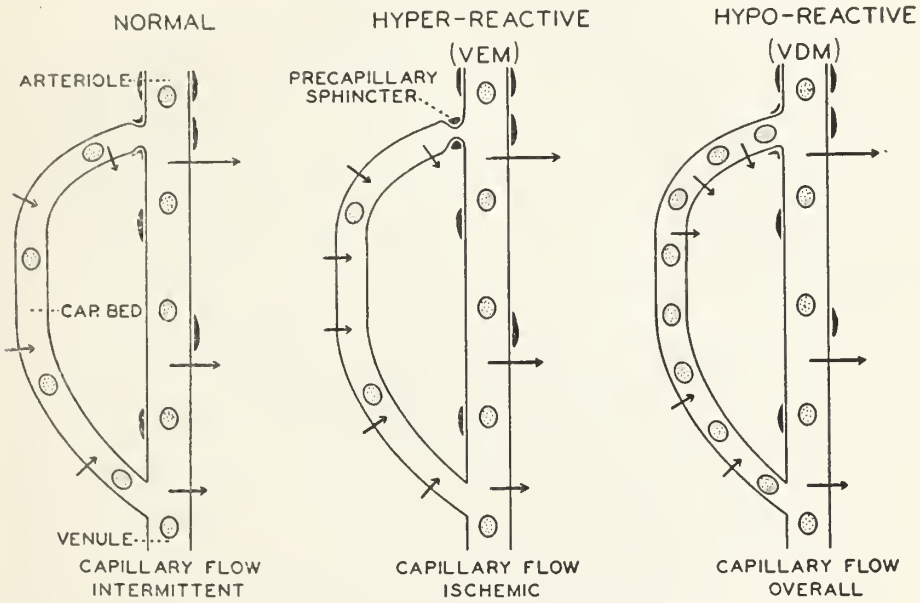

FIG. 3. Diagram of fluid exchange between blood and tissues

tail vein of the rat. The presence of a vasoexcitor principle is manifested by the development of a period of increased sensitivity to the constrictor effects of topical epinephrine. We have called substances which enhance the sensitivity of the precapillary sphincters, vasoexcitor materials, or VEM. Substances having opposite effects, recognized from the depression in epinephrine reactivity following their intravenous administration, are called vasodepressor materials, or VDM.

These vasoactive factors were found to originate in specific organs under specific metabolic conditions. Thus, the hepatic vasodepressor originally termed VDM, and since identified as ferritin, was found to originate chiefly in the liver and to arise normally only under anaerobic conditions, to judge from *in vitro* studies. Under aerobic conditions, none appeared; indeed, exposure of VDM to normal liver slices under these conditions rendered it physiologically inert. Of importance in tourniquet shock is the fact that skeletal muscle possesses the property of forming VDM under anaerobic conditions; but, unlike the liver, it cannot inactivate it aerobically. The kidney proved to be the sole source for VEM; and the same pattern of anaerobic formation and aerobic inactivation held for this renal vasoexcitor principle.

As I have mentioned, VDM of hepatic origin has been identified as the iron containing protein, ferritin, which in crystalline form gives a positive vasodepressor effect with as little as 0.0005 microgram N injected into a 120 gm. rat. The vascular activity of ferritin has been found to be related to the state of its thiol groups. It is inactive in the disulfide form, acquiring its vascular activity on reduction of these groups to the sulfhydryl form.

The crystallization of ferritin fortunately made it possible to develop antiferritin sera by injection of heterologous ferritin into rabbits and thus provided us with a valuable tool for use in our bioassay method. When both VEM and VDM are present together, the resulting effect on the vessels of the rat mesoappendix is dependent upon the relative concentrations of each factor. Indeed, a neutral assay may be given by biological fluids containing large but equivalent amounts of both VEM and VDM. By incubating such a mixture with antiferritin serum, all ferritin vasoactivity is abolished and the residual VEM activity can then exert its effect in the rat test. Conversely, any VEM present can be inactivated by incubation at 37.5° with normal kidney slices under aerobic conditions, thereby unmasking any ferritin present. These fractionation procedures proved of particular value in our study of hypertension.

We are now in a position to describe the manner in which VEM and VDM are involved in the evolution of the experimental shock syndrome. The findings with respect to the sequence of vascular and humoral events as seen in hemorrhagic shock induced by graded hemorrhage are presented in diagrammatic form in *Figure 4.* The initial compensatory response to blood loss is apparently related to a reduction in blood volume, the subsequent decompensatory phase to the period of inadequate peripheral blood flow. The compensatory response is characterized by a hyperreactive condition of the peripheral blood vessels as evidenced by an increase in the frequency and amplitude of the intermittent constrictor activity (vasomotion) of the metarterioles and precapillary sphincters and in their heightened reactivity to topically applied epinephrine. The resultant ischemia and restriction of peripheral blood flow to the most direct thoroughfare channels (see *Figure 2*) serve to maintain an active venous return of the blood from the tissues in the face of a reduced blood volume. As long as this type of vascular hyperreactivity persists, the animal can be recovered by the restoration of the blood lost. Bioassays of the blood taken during this phase of shock show the regular presence of VEM. This VEM can be shown to have its origin in the kidney and to result from the reduced renal blood flow secondary to the reduction in blood volume. Biopsies of the liver show no VDM activity in

the liver wash and there is chemical evidence that the liver is still maintaining an aerobic existence during this phase of shock.

On the other hand, with the development of an irreversible type of shock following prolonged drastic hypotension, a new set of vascular changes progressively appears in the mesentery and omentum, and finally disrupts the peripheral circulation. These changes are decompensatory in nature and are initially made evident by a progressive falling off of epinephrine reactivity and a slowing, and finally complete cessation of spontaneous vasomotion.

The loss of these restraining compensatory influences on the peripheral circulation results in the diversion of increasing amounts of blood into the capillary side channels from which it fails to return to the active circulation. This in turn leads to the eventual failure of the venous return to the heart and to peripheral circulatory collapse. Once this hyporeactive stage has fully developed, transfusions exert only a transient effect, a state of irreversibility to replacement therapy having been reached. The relation of these vascular changes to the blood-borne principles with which we have been concerned is depicted in *Figure 4*. The more drastic hypotension has led to the complete abolition of the blood flow. As a consequence, VEM, which is still being formed by the anaerobic kidney, is unable to reach the circulation and exert its compensatory effects on the peripheral vascular bed. Now the blood flow to the liver has been sufficiently reduced to shift its metabolic pattern from the aerobic state to one in which anaerobic processes are initiated. As a consequence, VDM formation

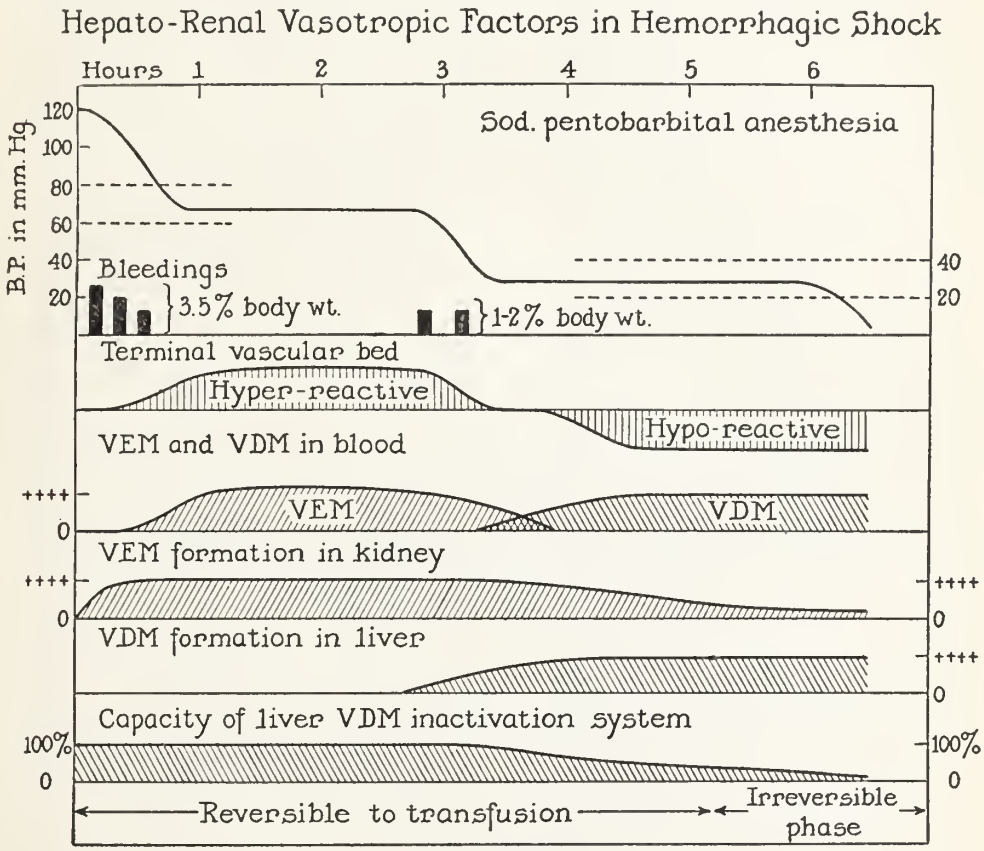

Fig. 4

begins and this vasodepressor appears in the circulation in increasing concentrations which soon predominate over the VEM still present in the blood stream. The capillary bed now comes under the control of the vasodepressor factor, with the consequences described above. The final link in the sequence of events leading to irreversibility is the progressive deterioration of the liver VDM inactivation system, which results from the prolonged unrelieved hypoxia which follows on the drastic hypotension. After 90 to 120 minutes of this hypoxia, the hepatic VDM inactivation system undergoes such deterioration that, when oxidative conditions are restored by a transfusion of the blood lost, the liver is unable to liberate the vascular bed from the decompensatory effects of VDM. Hence, this defect in the VDM inactivation mechanism may be regarded as the crucial one which underlies the development of the irreversible stage. In relating these hepatic VDM defects to the peripheral circulatory failure of irreversible shock, emphasis is placed on the effects of these derangements in diverting blood from the general circulation by its sequestration in the splanchnic viscera, particularly the liver and gut. The pooling in the liver is attributed to the vascular effects of the local concentrations of VDM in that organ and leads to increases in the intrahepatic and portal pressures which would, in turn, result in mesenteric stasis, intestinal congestion and hemorrhage. It is beyond the scope of this presentation to examine, in more detail, the considerations which have led to this concept of irreversible shock, and the reader is referred for them to other publications from this laboratory.

We may now turn to the experiments which have related these hepatorenal vasotropic factors to experimental renal and essential hypertension. Through the pioneer work of Goldblatt, it has become possible to induce, with regularity, a state of hypertension in animals by restricting the blood flow to the kidney by means of clamps applied to the renal arteries. Another method consists in the wrapping of kidneys with silk or collodion gauze. When this is done, hypertension develops and persists as long as the clamp or wrapping remains. Utilizing this type of experimental procedure, we have systematically investigated the VEM-VDM systems during the hypertensive syndrome by means of blood assays, as well as by studies *in vivo* and *in vitro* of VEM-VDM metabolism in the liver and kidney.

The results of these studies are presented in diagrammatic form in *Figure 5*. Within a very short time of the application of the Goldblatt clamp, VEM appears in the blood stream in mounting concentrations and persists throughout the acute stage of hypertension. At about the time blood pressure stabilizes at the chronic hypertensive levels, this factor can no longer be detected in unfractionated bloods, the blood usually giving a neutral reaction. Examination of the kidney *in vitro* shows that it has sustained a very specific defect in VEM metabolism as a result of which VEM formation, normally restricted to anaerobiosis, now takes place under aerobic conditions as well, and hence, continuously. The kidney is thus unable to regulate its release of this vasoactive factor. Why then does this factor disappear from the blood stream? The possibility was explored that there may be no actual disappearance of VEM but that its effects in the rat test might be neutralized by the concurrent appearance of the oppositely acting factor, VDM. When the procedures described above for fractionating mixtures of VDM and VEM were carried out, this was found to be the case. The liver, apparently in response to the high concentrations of humoral VEM, was now pouring out VDM in amounts which eventually were sufficient to set up a new equilibrium between these oppositely acting factors. *In vitro* studies of the liver from hypertensive animals showed that it was now releasing VDM under both aerobic and anaerobic conditions.

It was now of interest to see what the effect of these humoral changes might be on the capillary bed, with whose regulation these principles are concerned. Very striking changes were observed. In both the rat and dog there was found to develop a very profound hyperplasia of the mesenteric capillaries. In addition, these vessels manifested a marked

hyperreactivity as evidenced by their enhanced constrictor response to topical epinephrine; and in the rat, which lent itself to this type of experiment, there was a striking increase in the response of the mesenteric capillaries to the intravenous injection of renal VEM. These observations would suggest that a very significant alteration in the peripheral vascular pattern had occurred, presumably as a result of the high concentrations of these vasoactive principles in the blood. This altered vascular pattern, both structural and functional, should present a situation of hemodynamic significance for the organism.

As pointed out earlier in this presentation, the close integration between the capillary bed and the terminal arterioles must, of necessity, lead to appropriate compensatory reactions of the terminal arterioles to this altered capillary pattern, otherwise there would be a breakdown in circulatory homeostasis. It is in this way, we believe, that changes in the systemic blood pressure would ultimately result from the sequence of humoral and vascular events just described. We appreciate that it will be necessary to reenforce this concept with direct experimental evidence for the manner in which alterations in the capillary bed and behavior, resulting from these humoral derangements, affect systemic blood pressure; and such is the direction of our experimental program.

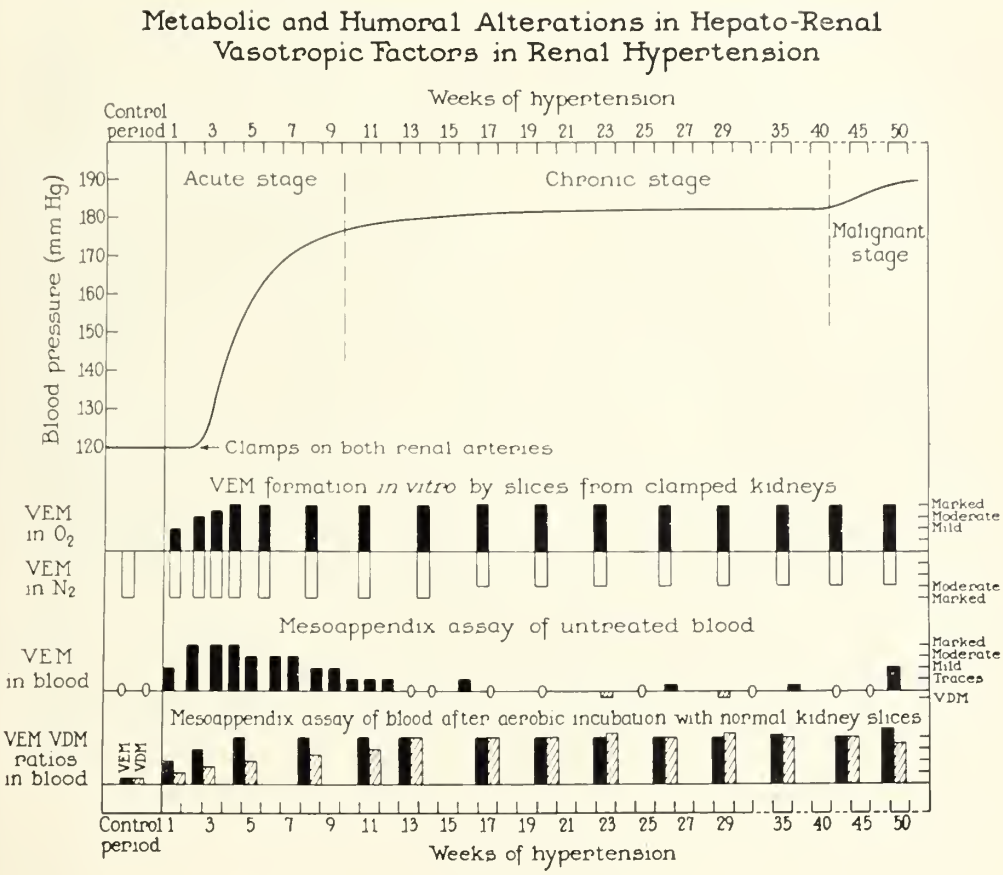

Fig. 5

Considerable supportive data have been obtained of an indirect character, favorable to this concept. For example, it has been found that there is a very direct relationship between the adrenal cortex, in whose absence hypertension cannot be induced by the experimental procedures described above, and the integrity

of the renal VEM mechanisms. The adrenalectomized animal, supported with salt alone, is unable to form VEM. It can do so, however, when given adrenal cortical extract or desoxycorticosterone acetate.

One final criterion has more recently been added to our study of hypertension. This is of a histochemical nature and consists in the use of a chemical compound 2,3,5-triphenyl tetrazolium chloride, which possesses interesting qualities. It serves as a hydrogen acceptor for intracellular reductases of the dehydrogenase family. On reduction by these intracellular enzymes, tetrazolium is changed from a water soluble colorless form to a water insoluble deep red substance, which is deposited intracellularly, presumably at the site of its enzymatic reduction. It thus serves to provide information as to both the intensity of enzymatic activity and the pattern of enzyme distribution within the cell. We have utilized this agent for the study of kidneys from normotensive and hypertensive animals. When a slice of normal kidney is incubated with this reagent for a period of one hour and the tissue fixed and frozen sections prepared, a characteristic picture is seen (*Figure 6*). The greatest accumulation of the deep red reduced tetrazolium takes place in the proximal convoluted tubules, where it is evenly dispersed as fine dust-like granules throughout the cytoplasm. In sharp contrast is the picture seen in the kidneys from renal hypertensive rats and dogs (*Figure 7*). In these kidneys, although the total amount of reduced tetrazolium is the same as in normotensive kidneys, it is deposited as heavy, coarse plaques and needles which are irregularly distributed in the cell. Evidently, in the proximal

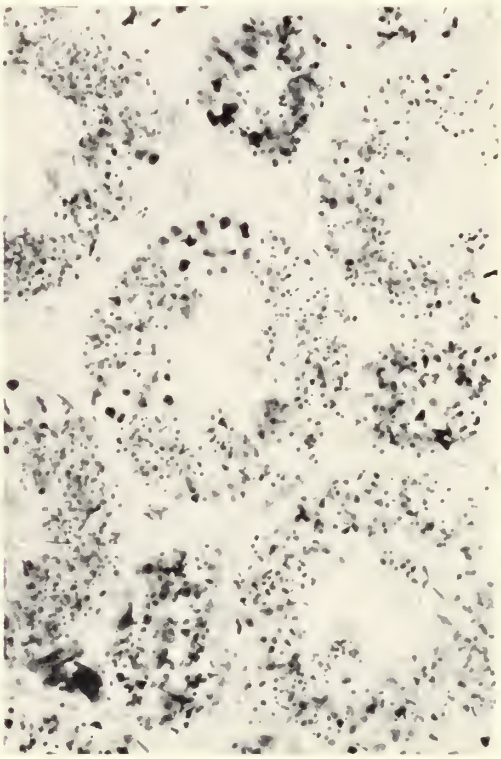

Fig. 6

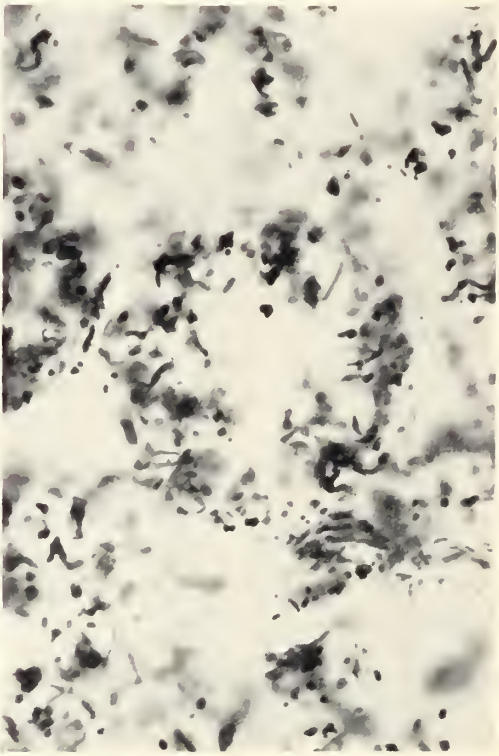

Fig. 7

FIG. 6. Section of kidney cortex of normotensive dog showing dust-like formazan granules in proximal convoluted tubules. (300X).

FIG. 7. Section of kidney cortex of hypertensive dog showing coarse plaques and clusters of formazan needles in proximal tubular cells. (300X).

convoluted tubules in renal hypertension there is a profound disturbance in the enzyme systems whose presence is revealed by tetrazolium.

This is, we believe, the first demonstration of a lesion of this character and is of particular interest for our concept of hypertension which would attribute the VEM defect in the kidney to a disturbance in an enzyme system, as yet unknown, which regulates VEM metabolism. Of particular significance, therefore, are the experiments which suggest a connection between this enzymatic defect and the renal VEM system. We have found that it is possible to change the VEM pattern of normal kidney to the hypertensive type by exposing the kidney to anaerobic conditions for approximately one hour, and then restoring aerobic conditions. As a result of this anaerobic pre-treatment, the normal kidney now produces VEM in oxygen as well as in nitrogen, just as does the hypertensive kidney. Tetrazolium studies of these pre-treated kidneys showed that in addition to assuming the hypertensive metabolic pattern, they exhibited the same tetrazolium pattern of deposition in the proximal convoluted tubules that is characteristic of the hypertensive kidney. The parallel development of the hypertensive metabolic and tetrazolium patterns in these previously normal kidneys is suggestive of a connection between the alterations in VEM metabolism and the enzymatic disturbance in the proximal convoluted tubules.

The significance of these data, obtained on animals with experimental hypertension, for an understanding of the mechanisms of human essential hypertension is dependent upon the extent to which the same derangements occur in essential hypertension. An assessment has therefore been made of the VEM-VDM mechanisms in human essential hypertension, utilizing the same procedures employed in animals. The similarity in the results argues strongly for a basic similarity between experimental renal hypertension and that occurring spontaneously in man. Bioassays of the blood from patients with chronic essential hypertension yield either neutral reactions or a slight preponderance of VEM, prior to fractionation. The fractionation procedures previously described show the regular presence of high titers of both VEM and VDM. A type of acute hypertension, that occurring in toxemia of pregnancy, was also studied, with the same findings of large amounts of VEM and VDM in the blood during the hypertensive episode. Opportunity was provided to study one case of hypertension due to unilateral kidney disease resulting from an aneurism of one renal artery. Prior to operative removal of the kidney, high titers of both VEM and VDM were found, with VEM predominance. On removal of the kidney, with a return to and a persistence of normotensive levels, both VEM and VDM disappeared from the circulation. Catheterizations of the renal and hepatic veins in hypertensive subjects have confirmed the renal and hepatic origins of VEM and VDM, respectively. Bioassays of human hypertensive kidneys permitted the *in vitro* study of VEM metabolism. In contrast with kidneys of normotensive patients which formed VEM only in nitrogen, hypertensive kidneys behaved as did the kidneys from hypertensive dogs and rats, forming VEM in both the presence and absence of oxygen.

TABLE 1

CRITERIA FOR EVALUATING HYPERTENSIVE SYNDROME

	RAT (PERI-NEPH.)	DOG (R. A. CLAMP)	HUMAN (ESSEN-TIAL)
1. Aerobic formation of VEM by kidney *in vivo*	—	+	+
2. Aerobic formation of VEM by kidney *in vitro*	+	+	+
3. VEM in blood during acute stage	+	+	+
4. VEM and VDM in blood during chronic stage	+	+	+
5. Vascular hyperreactivity to epinephrine	+	+	+
6. Vascular hyperreactivity to VEM	+	—	—
7. Hyperplasia of capillary bed	+	+	+
8. Renal histochemistry (Tetrazolium pattern)	+	+	+

It has, as yet, not been possible to study the mesenteric capillaries in the human hyper-

tensive subject. However, Dr. Richard E. Lee of our laboratory has carried out studies on the conjunctival capillary bed in normotensive and hypertensive subjects. The architecture of this capillary bed is in its essentials similar to that of the mesentery of the dog and rat. As in the experimental animals, there was a striking contrast between the capillary structure and behavior of normotensive and hypertensive subjects. The hypertensive subjects showed a similar hyperplasia to that noted in the hypertensive dog and rat, with elongation and tortuosity of the true capillaries. They also showed a ten-fold greater sensitivity of the constrictor response to the topical application of epinephrine than is characteristic of the normotensive subject.

Finally, the tetrazolium patterns of the renal cortex, of biopsy specimens obtained at operation from normotensive and hypertensive subjects, were indistinguishable from those seen in the normotensive and renal hypertensive dog and rat. The hypertensive patient had the same distorted pattern of deposition of the reduced tetrazolium as was uniformly seen in the hypertensive dog.

In *Table 1* there are assembled the various criteria, relating to the VEM-VDM systems and the capillary bed, which have been employed in our analysis of experimental renal hypertension in the dog and rat and human essential hypertension. The resemblance between the experimental and the spontaneous human hypertensive states constitutes strong evidence of a basic similarity between them and has important implications, some of which may be pointed out. In the first place, it reenforces the validity of the experimental aproach to hypertension which uses renal arterial constriction or perinephric wrapping as the means of producing experimental hypertension. Secondly, it would seem to favor the existence of a specific alteration in renal metabolism in both human essential and experimental renal hypertension. Support is provided, furthermore, for the localization of this defect in the proximal convoluted tubule and for its being of enzymatic character.

Before closing I should like to summarize briefly the evidence at hand for the participation of the angiotropic factors, VEM-VDM, in experimental renal hypertension. These factors appear in regular sequence in the blood of dogs and rats made hypertensive either by perinephric wrapping or renal artery constriction. The appearance of VEM and VDM in the blood has been shown to arise from derangements in the renal and hepatic mechanisms which regulate the metabolism of these factors. Similar derangements can be produced *in vitro* by a brief exposure of these tissues to hypoxia. These changes in VEM and VDM metabolism are paralleled by structural and functional alterations in the terminal vascular bed with whose regulation these principles are concerned. There is a pronounced hyperplasia of the capillary bed and an enhanced reactivity. The functional and structural characteristics of the terminal vascular bed have been discussed and their importance for circulatory homeostasis pointed out. The high degree of integration of the activity of the terminal vascular bed with the central blood vessels more directly responsible for blood pressure regulation, suggests that the altered condition of the capillary bed observed in experimental renal hypertension and presumably dependent upon the altered VEM-VDM titers in the blood stream, may be a contributing factor in the genesis and maintenance of the hypertensive syndrome. The same considerations apply to human essential hypertension.

In a broader sense, these two angiotropic principles may be considered to constitute a homeostatic system which participates in the regulation of the peripheral circulation. The extension of studies of this type to other circulatory disturbances can be expected to reveal their participation in other derangements of the circulation, if our inference is valid as to the general significance of these humoral factors. Studies now under way on cirrhosis, nephrosis and heart failure are making it clear that this is, indeed, the case, but it would be beyond the scope of this presentation to extend it to a consideration of these allied problems.

Newer Developments in Venereal Disease Control in the United States and Abroad*

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PROGRESS from the scientific medical treatment and research standpoint has been so rapid in the venereal disease field in the last seven or eight years that much which was considered standard practice only a short time ago has been abandoned, revised or subjected to the closest scrutiny. Many of these changes have been orderly and natural, but a few have been sufficiently drastic to give rise to differences in opinion in public health practice and to sudden shifts in administrative viewpoint which have left confused thinking and unfortunately at times unwarranted curtailment and budgetary restrictions in their wake. We are, moreover, at the moment confronted with the very real prospect of national mobilization, and with the past experience which indicates that such social, economic and moral crises are always accompanied by a marked upsurge in gonorrhea, syphilis and the other venereal diseases. It is very appropriate, therefore, it seems to me, to present to you, for whatever implications they may have in our local situation, some of the problems which are being discussed at national and international level.

BASIC DEVELOPMENTS IN THE LAST DECADE

At the outset I would like to remind you, by way of background, that only ten years ago not one of the venereal diseases had completely satisfactory treatment. In spite of major health department effort and expenditures less than one-fourth of patients with syphilis in this country completed the long course of medical observation and treatment essential to insure cure of the disease. Initial courses of the sulfonamides cured hardly more than one-half of the patients with acute gonorrhea. We were still talking about and recommending such a drastic, dangerous and expensive procedure as fever therapy for treatment resistant gonorrhea, relapsing infectious syphilis, and for central nervous system involvement with Spirochaeta pallida. Available remedies were ineffectual for lymphogranuloma venereum, except, perhaps, in the earliest stages of the disease, which from the practical standpoint were seldom seen. Most patients with granuloma inguinale underwent months and years of debilitation in spite of every known medical, surgical and health procedure, all of which did relatively little to modify the natural course of the disease. During the last war and through the post war adjustment period there was a slow but steady increase in all types of recognized venereal disease in those parts of the world where adequate record keeping was available.

Now, just a decade later, in standard public health practice, 98 percent of all patients with syphilis who come under observation complete their treatment. This is, moreover, accomplished usually within a two week period. Public Health Centers which had large treatment clinics because of the accumulation of infected individuals requiring long courses of therapy and medical observation, often with totals of several hundred patient visits per day, in the densely populated areas, now have 10, 15 or 20 patient visits. Major health depart-

* Read before The College of Physicians of Philadelphia, Section on Public Health, Preventive and Industrial Medicine, 19 January 1951.

ment expenditures for record keeping and personnel, formerly required for attendance follow-up to keep track of patients until they were rendered noninfectious or cured, are now almost completely unnecessary. At present patients are cured so rapidly that normal epidemiologic procedures are neither quick enough or sufficiently effective to prevent immediate reinfection with gonorrhea and syphilis from becoming a common observation. Emphasis has changed completely from case holding to prevention in the broadest sense, including educational procedures, social study and case finding in all its aspects, but with particular emphasis on epidemiology and contact tracing.

It is, moreover, established that better than 95 percent of gonorrhea may be cured in a single treatment patient visit and that the majority of patients with lymphogranuloma venereum and granuloma inguinale may have their disease arrested with streptomycin, aureomycin or perhaps treatment with some of the newer antibiotics, carried out over a two week period or less. It is conceded by almost every authority in the field, at the present time, that fever therapy has no place in the treatment of gonorrhea or syphilis even with central nervous system involvement. The one possible minor exception to this is in the management of interstitial keratitis from congenital syphilis, where both the underlying factors causing the disease and the purpose of the treatment present a special case.

In the last two years the decrease in the number of fresh infections of both gonorrhea and syphilis in the United States has been so rapid as to confound health authorities. With diseases like these, which traditionally, because of ignorance, prejudice and association with morals have remained predominantly submerged, a reduced morbidity reporting need not necessarily reflect a true downward trend in the total population. In the past increased efforts vigorously but injudiciously applied, have all too frequently been known to result in less rather than more venereal disease coming under medical care. It is becoming evident, however, that this decrease is real when we consider as prime factors that there is less venereal disease in the younger age groups, that there are relatively fewer cases of infectious syphilis being found in spite of continued high discovery rates for late syphilis in older age groups and that the morbidity rates per 1,000 population for both syphilis and gonorrhea are decreasing, while the number of diagnostic observations per annum is increasing.

THE WORLD HEALTH ORGANIZATION STUDIES

Perhaps the greatest contribution of the World Health Organization of the United Nations, with which I was recently associated as Special Consultant on travel status, is in bringing the factors which have been found effective in venereal disease control in good health practice to play in those sections of the world where the venereal diseases remain a real threat to the family and even to the economy. Venereal disease is truly a world wide problem. In just a few places have these infections been reasonably effectively controlled and then only from constant vigilance. In many tropical and semitropical countries the health authorities are confronted not only with syphilis (and the other venereal diseases) but also with yaws, Pinta and in the near East with Bejal which are of equal or greater importance. The World Health Organization has accordingly reclassified these diseases in a more logical way from its standpoint and is currently organizing its campaigns for the detection and the treatment of the treponematoses. Considering the overall world problem and the similarity in the diagnosis, treatment and general management of the treponematoses, this approach is more logical and will almost certainly receive universal acceptance.

The prevalence and incapacitation, infant mortality and associated misery caused by the treponematoses in some parts of the world is almost unbelievable. Even in Europe the effect of war and of social unrest is readily apparent. To avoid criticism I do not want to compare in any detail the situation in one country with that in another, since in all the medical

and health authorities are putting forth their best efforts to combat a most difficult problem, frequently without the best support or resource; but I believe it might not be out of the way to remark that the venereal diseases are obviously more prevalent in countries like Finland, Poland, Yugoslavia, Germany, Italy and Greece, which have experienced greater disruption of their internal affairs than they are in Norway, Sweden, Denmark and Switzerland, which have seemed to maintain a more stable home front and family life.

Even Sweden, however, which was not actually invaded, has reflected the effect of the unsettled conditions in the surrounding countries. The incidence of syphilis in Sweden by the end of World War II (2.05 per 10,000 population) was almost five times that of 1941 (0.41 per 10,000 population), and in 1949 was still more than twice the prewar level. Gonorrhea in Sweden also more than doubled during the war and at its peak stood at 30.08 per 10,000 population. Principal attention in Europe has been given by the World Health Organization to the study of problems in Poland, Czechoslovakia, Bulgaria, Yugoslavia, Hungary, Italy and Finland. The importance of the Rhine River shipping in the dissemination of venereal disease has also been recognized and a commission of experts from Switzerland, France, Belgium, the Netherlands and from the French, British and American zones of Germany, have already formulated methods of control. Some 80,000 migrant workers (boatmen and their families) are concerned. Particularly fine clinical and epidemiologic facilities have been developed in conjunction with this program by Dr. E. H. Hermans in the port of Rotterdam which I had the opportunity to study in some detail.

By comparison with the situation in the near East, far East and some other parts of the world, these problems just mentioned, however important, seem insignificant. The areas of greatest concentration of effort in this field by the World Health Organization are in Egypt, the near East, India, the Philippines and Haiti. In these places it is necessary for the World Health Organization to be concerned not only with conferences, formulation of policy and surveys, but also with actual demonstration of diagnostic and treatment procedures. In this program fully equipped and functioning teams are sent into areas where there is a reasonable assurance that the local Health Department and medical personnel will continue to carry on the work when the demonstration is completed. Such demonstration units will usually function for periods of from one to three years.

Surveys in Haiti, for example, show one-fourth of the population to be suffering from syphilis and gonorrhea and 85 percent to be afflicted with yaws. In the Philippines extensive surveys have shown that syphilis rates among the pregnant women are between 140 and 170 per 1,000 population. Dr. J. C. Cutler, in charge of one of the WHO teams working in the North of India, with whom I had the opportunity of personal conference, states that in Simla 70 percent of the adult population studied were found to be infected with syphilis. In Jind, north of Delhi, another area surveyed, one-half of the population had positive blood tests for syphilis. Such figures as these are applicable, I understand, for the prevalence of syphilis over much of the far East.

As might be expected, the major problem is one of basic medical care. Among 35,000 new admissions for venereal disease per annum in Calcutta, less than one-half received even the basic essential diagnostic aid of a blood test for syphilis, because the present facilities are inadequate for the patient load. In spite of the prevalence figures just given, less than 15 percent of the population of India has been studied, and it will be years before there are sufficient personnel or drugs to adequately treat even the patients that are being discovered. So little penicillin is available, for example, that one of the expert teams was able to give as complete treatment a total dose of only one injection of 300,000 units of penicillin to each patient discovered to have syphilis. In the large University clinic at Mad-

ras, serving a population of several millions, it has been standard practice, because of lack of supplies, to treat with penicillin only those syphilitic pregnant women who have active infections with lesions in the last months of pregnancy; the rest received no penicillin.

So I could go on with example after example, but I believe such discussion serves no purpose other than to point up the fact that, the venereal diseases are major problems of world wide scope, controlled only in limited areas and then by a *sustained* high standard of public health practice with adequate resources.

STUDIES IN THE IMMUNOLOGY OF SYPHILIS OF PUBLIC HEALTH IMPORTANCE

Although the most striking advances in the control of the venereal diseases have been in terms of treatment, one development in the field of immunology is worthy of note because of its wide spread implications. This is the discovery by Nelson and Mayer* of a hitherto undetected antibody in the serum of syphilitic experimental animals and in human patients which will immobilize virulent living Treponema pallidum in vitro. It has long been recognized that the present serologic tests for syphilis carried out with lipid antigens of mammalian tissues, even though they detect the disease with a high degree of specificity are not an actual index of immunity. Many aspects of treatment and control have of necessity been guided by somewhat arbitrary standards based on clinical experience with large numbers of cases, since decisions in terms of the individual patients were often impossible. A procedure, therefore, which may tie the disease status of the patient more closely to the blood test procedure cannot fail to result in a more rational handling of the patient from both the medical and public health standpoint.

THE SIMPLIFICATION OF SYPHILIS THERAPY

Within the last year or two, the treatment of syphilis is becoming more and more simplified in terms of cost, health department surveillance and treatment patient visits required. This has resulted from improvement of the absorption delaying vehicles for penicillin which have gradually come to produce longer and longer sustained effective blood levels. The treatment of syphilis, which, from 1943 to 1946 required a week to ten days of hospitalization and from 1946 to 1950 required at least once daily injection of a slowly absorbed penicillin perhaps on an ambulatory basis, is now normally given every other day or every third day with equally satisfactory therapeutic results. For all stages of syphilis except some of the more serious (and presumably more refractory) late stages it is customary to give a total dose of approximately six million Oxford units, often in five individual intramuscular injections of 1.2 million Oxford units each at 2 to 3 day intervals of procaine penicillin G in absorption delaying vehicle. The cure rate from such therapy is variously estimated, but the conclusions reached in the international congresses indicate that it is well over ninety percent.

DEVELOPMENT OF TREATMENT PROPHYLAXIS

Another important development has been in the prophylaxis of syphilis by penicillin therapy. It has been shown that relatively small doses of penicillin, in the magnitude of 1.2 million Oxford units are capable of curing a large number of patients with syphilis, during the incubation period or early in the course of their disease. Application of this observation has been made in two ways in the public health field. First, realizing that syphilis and gonorrhea may be acquired simultaneously, there is an increasing tendency to treat all patients with acute gonorrhea with not less than 1.2 million Oxford units of penicillin in an absorption delaying vehicle, usually in a single injection, to cure concurrently acquired syphilis. Secondly, it has been shown that routine treatment of persons who have been recently exposed to infectious lesions of syphilis but who have not as yet developed symptoms, with approximately 1.2 million Oxford units of penicillin will prevent the development of syphilis

* Nelson, R. A. and Mayer, M. D. Immobilization of Treponema pallidum in Vitro by Antibody Produced in Syphilitic Infection, J. Exper. Med. **89:** 369 (April) 1949.

in all but about 4 percent of cases. Control series with identical groups of patients have revealed that 60 to 70 percent of individuals normally exposed to infectious syphilis under similar circumstances will acquire the disease. There can be no doubt, therefore, that such immediate treatment of exposed individuals or suspects will cure the majority of patients in the incubation period. The use of this procedure is not at present standard public health practice but deserves serious consideration. A patient who is brought under health department observation from epidemiologic procedure and who is treated before he develops infectious lesions does not have much chance to disseminate the disease in the community.

THE ERADICATION OF CONGENITAL SYPHILIS

Within the last year, on both a national and international basis, considerable emphasis has been placed upon the complete eradication of congenital syphilis. With penicillin therapy this becomes a distinct possibility if it can be universally applied. Effective treatment with penicillin given the syphilitic pregnant woman in any stage of her disease, it is generally agreed by experts and demonstrated by local studies, has reduced the possibility of giving birth to an infected infant to the magnitude of one percent or less. Almost all infantile congenital syphilis occurring in Philadelphia at the present time and in other areas where medical practice is good, comes from inadequate prenatal care, in which no opportunity for diagnosis and treatment of syphilis is afforded prior to delivery. These are failures in community organization and administration or in health education rather than in public health procedure. H. G. Irvine, Venereal Disease Control Officer of Minnesota, where an effective control program has been in operation under his guidance for the last thirty years, reports that in 1949 there was *one* case of congenital syphilis in that state among 73,627 live births. Minnesota is admittedly in a low prevalence area for venereal disease and with stable rural population is not subject to many of the stresses of a large densely populated coast city or industrial area. Nonetheless, this goal is within the grasp of every health department and should be reached in most places before too many years.

BASIC MAINTENANCE CONTROL PROGRAM FOR THE VENEREAL DISEASES

I would like to round out and complete my discussion with just a few words about what is probably the livest topic in venereal disease control in public health administrative circles today, namely, the *basic maintenance control* program. With the venereal diseases we have come to a situation which is almost unique in public health practice. In a fifteen year period in the United States, since the National Venereal Disease Control Program was launched in 1936, without the use of any immunizing procedure, employing epidemiology, in its broadest sense, and treatment alone, a group of infectious, readily communicable, widespread diseases have been reduced to the point where we may talk about a controllable minimum number of cases.

On a national basis, for the last three years, the morbidity from early syphilis has been consistently and steeply downward. For the last half of 1950 it was 12 percent below the corresponding period for the previous year. This decrease in morbidity obtained in a period when the number of diagnostic observations for syphilis was increased by more than 500,000 per annum.

What is meant by a controllable minimum number of cases? It is realized that for syphilis and gonorrhea, where immunizing procedures are not available, it will probably never be possible in densely populated areas to approach the zero point in incidence as with smallpox, typhoid fever or diphtheria. It is felt, however, that a goal of one case of syphilis per five thousand population per annum is not unreasonable and is attainable. There are at least nine states in the United States who have already reached this figure. They are Idaho, Massachusetts, Minnesota, New Hampshire, North Dakota, Oregon, Rhode Island, Utah

and Wisconsin. In fact, Norway, Sweden and Denmark have in their most favorable years reduced the incidence of syphilis to less than one case in 10,000 population. On the basis of the present population of the United States the controllable minimum number of cases of newly acquired syphilis always to be cared for, year after year, would be 30,000.

This is not an insignificant figure, but is one that requires rather careful program planning if it is to be effectively and economically handled. This is especially true when we know that for each case of undetected fresh syphilis an average of three additional cases will appear within a period of a few months; when we see, as was mentioned previously with respect to Sweden, that even after maintenance control was reached, unsettled world conditions caused a five fold increase in incidence in as many years, and when we realize that we are having free commerce and troop movements in parts of the world where effective control of the venereal diseases has hardly been started.

The declining incidence of syphilis and gonorrhea has already made it difficult for the Public Health Service to justify financial support of its program at the same level. Within the last year there was a marked reduction, somewhat arbitrarily applied, of Federal-State Grant-in-Aid Funds for Venereal Disease, which has resulted in sharp curtailment of control activities to the point of virtual cessation of the program entirely, in some areas.

There are two types of thinking which I have come across at the national and international meetings which are detrimental to our health objectives in reaching a basic maintenance control program and which I would like to pass on to you with the reasons why they are not acceptable. The first of these is a general line of thinking as follows: The venereal diseases are declining, their treatment is effective, since the downward trend has commenced the venereal diseases will tend to disappear naturally in the course of time and, therefore, special effort is no longer necessary. The second analysis is on a statistical and fiscal basis and is somewhat pernicious because superficially it seems logical until the suggested program is examined in some detail. This approach determines the current cost of treatment of a case of syphilis by dividing the total number of cases occurring in the community in any one year into the total cost of the program for the same period. The amount of money necessary for future operation is then determined by projecting the graph of this downward trend in incidence a year or more in advance, reading off the number of cases to be anticipated, and finally multiplying this figure by the previously determined cost per case.

In Philadelphia the incidence of infectious syphilis is still six times the figure predicted at basic maintenance control level. With respect to the first argument above to relax the venereal disease control program before the maintenance control level is reached or closely approached will merely result in a gradual increase in the amount of venereal disease. This increase is pernicious in that it is slow and hard to detect. Even were spot checking through case finding procedures possible, the upward trend would not be evident for two or three years and then it would not be reversed by prompt reactivation of the program for another two or three years. This was seen to be the case in Scandinavian countries which I have cited and has also been amply demonstrated in this country in which the peak in the incidence of venereal disease caused by World War II was not arrived at during the war but only in 1946 and 1947. Especially to be feared, if curtailment in the program includes decrease in epidemiology and other case finding efforts which would almost inevitably be the case, is the fact that the Department of Health and the citizens of the area would not even be aware of the increasing incidence of venereal disease as it occurs. These diseases have always remained hidden without special health department effort to bring them to light.

Some of the more progressive health departments, to meet these threats, have made careful cost analyses at the request of the Public Health Service. In the State of Tennessee, for

example, it has been found that the cost of care of each fresh case of syphilis is $124.46 per annum. In Chicago this cost is $180.45 per case per annum. The similar cost figure for Philadelphia is $172.78 per case per annum (based upon the 1950 case load of 2,417 new patients with early syphilis during that year). These cost data cover all services to these patients, such as health education, case finding, epidemiology, laboratory examinations, medical diagnosis, treatment and follow-up visits. The fact which has been lost sight of in some of the current thinking in program planning is the expression of the law of diminishing returns which becomes inevitable as the infection comes under control. On a national basis, at present, in order to find one case of syphilis an average of 11.3 diagnostic observations are required. As the disease becomes less prevalent, these figures will increase. Six years ago during World War II, when the number of fresh infections with syphilis in Philadelphia was double the current figure, the cost of care for each case of early syphilis per annum was in the magnitude of $45.00. *Maintenance Control Level* in Philadelphia would be reached at between 400 and 500 patients with early syphilis per annum. A careful and realistic estimate of the cost per patient per annum at this level would be $416.73. I go into this much detail to emphasize that, even though the overall cost of venereal disease control will be substantially less as these diseases diminish in frequency in the population, the law of diminishing returns must be reckoned with. A reduction in the case load in Philadelphia, from its present level (1950) of 2,417 patients with early syphilis per annum to an estimated maintenance control level of 414 patients per annum will result in a reduction in cost not to one-sixth of the previous total annual expenditures, as would be indicated by consideration of the case load alone, but to about 41 percent of this total (from the current level of about $415,000 to an estimated $175,000 per annum).

When we begin to talk about a case load of about 500 patients with early syphilis per annum, and to an unknown though relatively small case load of patients with late syphilis, gonorrhea and other venereal diseases, it becomes evident that many remarkable changes in program planning are essential. With an average discovery rate, the equivalent of one patient per practicing physician in the community every six years, syphilis treatment as such ceases to be a problem. Health education, case finding and epidemiology, on the other hand, are still of major importance and will take up approximately two-thirds of the expenditures essential to proper venereal disease control. It will be immediately recognized that this is the type of transition which fits readily into the shift from the special health service to the generalized program such as is gradually being adopted throughout the country at the present time. Case finding would readily become a part of the general health maintenance clinic with its generalized medical and nursing staff and could be most economically carried out in this way, provided the proportionate amount of time necessary to do an adequate job in venereal disease control were given and paid for. I mention this last item "paid for" in particular since in many areas of decreasing venereal disease prevalence in the United States there is already a tendency to remove the specialized venereal disease nurse, physician or investigator and to provide no counterpart or increase in staff to take up this additional load. The additional load is placed as just one more duty on an already overworked personnel.

One could speculate as to how long it might take to reach maintenance control level of the venereal diseases in this city or throughout the United States. The fact that it has been reached in isolated instances throughout the world and in a few states in this country indicates that this is a specialized and local problem influenced by a number of factors, to which now one additional all important consideration has been added, namely, mobilization and the troubled condition of the world. It has been estimated by some of the best health authorities that basic maintenance control for the venereal diseases in the United

States could be accomplished in a five year period were it not for the present emergency situation. Under existing circumstances the most that can be said is that the control of the venereal diseases in the United States is in sight. Yet, in spite of currently favorable downward trends in the incidence of syphilis and gonorrhea, curtailment in program is unwise until the small case loads of basic maintenance control are approached, or actually reached. Finally, it must be borne in mind that problems of venereal disease are highly specific to the area concerned so that allocations and generalizations at national or state level have very limited and often doubtful application to the local program.

Memoir of R. Max Goepp*

By HARRISON F. FLIPPIN

Rudolf Maximilian Goepp, M.D., the youngest of seven children, was born in Tompkinsville, New York, on October 31, 1866 and died in Philadelphia on May 19, 1950.

At an early age he was taken to live in Germany, the land of his paternal Moravian forebears. There he received his primary education and, at the age of twelve, was sent to a boarding school in Switzerland. He remained in Switzerland a little over a year when he returned to the United States and began to prepare himself for college in New York City. At the age of fifteen, because of lack of funds, he was compelled to stop school and found employment as a clerk in a store. Two years later he entered Harvard College, working his way by tutoring his classmates in French and German. He found this quite difficult and, after one year, he decided to go west and grow up with the country. The following nine years of his life were filled with the adventure of the growing west. During this time he lived as a cattle rancher in Colorado, a fruit rancher in California, and worked as a book-salesman throughout the Texas Panhandle. After this experience, he concluded that after all there were more interesting pursuits in the world than those of grazier, agriculturist, or drummer and, therefore, decided to return east for more formal education.

In 1893 he came to Philadelphia, having obtained a position teaching German, French, and Latin at the DeLancey School for Boys and, later, at the Chestnut Hill Academy. After four years of teaching, he enrolled as a student at the University of Pennsylvania, graduating in the medical class of 1900. Immediately after completing his interneship at the Philadelphia Polyclinic Hospital, he accepted a position for the summer as superintendent of a camp for children who had been moved out of the Philadelphia Orphan Asylum, at Overbrook, because of an epidemic of diphtheria. After this job was finished, he contracted a severe attack of typhoid fever, during which he received 45 tub baths, which constituted a record, and experienced a loss of body weight from 145 lbs. to 115 lbs. On his recovery from this illness, which lasted several months, Dr. Goepp entered the private practice of medicine and at the same time began a brilliant academic career, which started with his appointment as assistant to Dr. Solomon Solis-Cohen, at the Jefferson Medical School, the Graduate School of the Philadelphia Polyclinic Hospital, and at Blockley. It was at Blockley that he did most of his teaching and acquired his keen interest and rare ability in diagnosis.

In 1904, Dr. Goepp was appointed Dean of the Graduate School of the Philadelphia Polyclinic Hospital and held that position until the institution was absorbed by the University of Pennsylvania, in 1918. At various times he held professorships at the Graduate School of the University of Pennsylvania, the Jefferson Medical College, and the Woman's Medical College. He also held the position of Medical Referee of the Aetna Life Insurance Company for 43 years and was a Medical Consultant for the First National Bank of Philadelphia.

Dr. Goepp was the author of many scientific papers and books. During his early years in practice, he supplemented his income by translating a number of medical textbooks from the French and German. He published several original text-books, the best known being those dealing with medical, dental, and nurses State Board questions and answers. It was in the preparation of the 8th Edition of The Medical State Board Questions and Answers that I came to know and appreciate the man. Throughout the days that we worked on his

* Prepared and printed at the request of the Council of the College of Physicians of Philadelphia.

book, one could but marvel at his intense interest in the many new developments in medicine and his great desire to see the work completed. I am happy to say that this was accomplished.

An illustration of Dr. Goepp's versatility was that early in his career, the managers of the Stephen Girard Estate engaged him to translate Girard's French correspondence, in order that it could be used in a biography. This work occupied him as an avocation for approximately two years.

Although Dr. Goepp enjoyed people and found great satisfaction in the diagnosis and treatment of disease, his love of writing and teaching was indulged to the sacrifice of his private practice. However, those patients that he did accept, received his complete interest and sympathy, as well as the benefit of his excellent medical judgment.

Despite the fact that Dr. Goepp was a very busy man, he always found time for his family. It was in his home that he pursued one of his chief hobbies, carpentry, which was rivalled only by his great love for literature, politics, and world affairs. During his life he experienced a number of personal sorrows, the outstanding of which were the sudden death of his first wife, Josephine Pyle, in 1913, and the loss of his son, Max, Jr., at the age of forty-two, in an air crash in Newfoundland, while on a special government mission, in 1946.

Dr. Goepp is survived by his widow, Alice Philippa Cloughley; two sons, Dr. Philip Henry Goepp, II, of Rochester, N. Y., and Robert H. Goepp, of Philadelphia; and four daughters, Miss Katherine and Miss A. Patricia Goepp, of Philadelphia, Mrs. Ross Scanlan, of Douglaston, Long Island, and Mrs. Colin Herrick, of Honolulu.

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Adrenal Cortical Activity and the Hypersensitive State: Some Clinical and Experimental Observations*

By A. McGEHEE HARVEY, M.D.

Professor of Medicine, Johns Hopkins University, School of Medicine

SINCE the studies of von Pirquet on serum sickness were reported in the early part of this century interest in the hypersensitive state as a factor in certain human diseases has become widespread. Although the clinical manifestations of allergy are very diverse, the specificity which is so characteristic makes it unlikely that there are many fundamentally different mechanisms by means of which the tissues react to various allergens. The production of antibody sets the stage for the allergic inflammatory reaction that results from contact with the exciting antigen. In addition to such well known examples as serum sickness, asthma, and drug hypersensitivity where the antigenic substance is known and a specific relationship can be established evidence has been accumulating that the anaphylactic type of hypersensitivity may play a role in the pathogenesis of certain other diseases. In 1913 Weintraud (1) made the suggestion that the lesions of rheumatic fever resulted from an anaphylactic reaction to bacterial products liberated in the tissues of the patient sensitized by infection. In 1925 Gruber (2) suggested that periarteritis nodosa might be due to hypersensitivity and later Vaubel found lesions which he compared to those of periarteritis nodosa in animals who received injections of a foreign protein. In 1937 Clark and Kaplan (3) noted vascular lesions in patients having serum sickness just before death and widespread periarteritis nodosa was found by Eason and Carpenter (4) in a patient who died nineteen days after the onset of serum disease. However, until the widespread use of sulfonamides greatly increased the opportunity for pathological study of the effects of the serum sickness type of anaphylaxis on human tissues this relationship was not amply documented. Rich and Gregory (5) presented conclusive evidence that the periarteritis nodosa seen in a variety of drug and foreign protein reactions is a manifestation of anaphylactic hypersensitivity. In addition, these workers were able to produce with regularity widespread lesions typical of periarteritis nodosa in rabbits by inducing a sensitivity reaction to horse serum. In the hearts of some of these experimental animals Rich and Gregory encountered lesions which

* Mary Scott Newbold Lecture LXIV, The College of Physicians of Philadelphia, 3 January 1951.

were very similar in their anatomic characteristics to those seen in patients dying with rheumatic carditis. Rich at that time reemphasized the fact that rheumatic fever and disseminated lupus erythematosus displayed a very impressive group of manifestations which occur as a part of the anaphylactic reaction in serum sickness. These important observations of Rich and others emphasized the need for a better understanding of the basic mechanisms of hypersensitivity, and the need for careful investigation of the possible role of sensitization in the pathogenesis of a wide variety of human diseases.

When the work of Hench and his coworkers (6) was announced it was felt that the relationships which have just been described indicated that adrenocorticotropic hormone (ACTH) and cortisone might be important tools in the study of various hypersensitivity reactions. The first patient treated was one critically ill with exfoliative dermatitis due to iodine hypersensitivity and the result was dramatic. This led to the development of a program for testing the clinical effects of ACTH and cortisone in hypersensitivity reactions due to a wide variety of antigens affecting different "shock organs", and in those diseases having a variety of phenomena in common with serum sickness of the anaphylactic type. Certain of the clinical studies will be outlined in the first part of the lecture and the remainder of the time will be devoted to certain experimental studies of interest.

During the 18 months since the successful treatment of the patient with exfoliative dermatitis due to iodine, many patients with hypersensitivity reactions to a wide variety of drugs have received ACTH or cortisone. Delayed anaphylactic reactions to penicillin of the serum sickness type may persist for several weeks after discontinuance of the drug. With suitable doses of ACTH there is dramatic relief of fever, arthritis, urticaria and angioneurotic edema within a few hours. Recurrence of urticaria five to fourteen days after stopping ACTH in many cases indicates that the improvement is not coincidental and that the sensitivity itself has not been eliminated. Irritation of the conjunctiva, lids and adjacent cutaneous surfaces following the instillation of various alkaloids into the eye has long been a recognized clinical entity. The same type of reaction will appear in 24 to 48 hours after a cutaneous patch test with an ointment containing the alkaloid. Several patients with such a reaction to atropine have been treated with ACTH with rapid healing of the lesions. Atropine therapy was reinstituted during ACTH administration without reaction until the dose of the hormone was lowered to 20 mgm. a day. The strongly positive reaction to the cutaneous application of atropine was blocked while the patient was receiving ACTH. Many other examples could be cited, such as instances of reaction to tetanus antitoxin and sulfonamides. Only one other, however, seems sufficiently important to relate in detail, the case of a 63 year old diabetic with insulin resistance who was treated with ACTH. A known diabetic since 1944 he had been readily controlled by diet alone until August, 1949. In January, 1950 glycosuria and weight loss progressed in spite of steadily increasing doses of insulin up to 500 units daily. After a period of weeks there was a spontaneous remission of the resistant state and a dose of 60 units daily was sufficient.

He was readmitted in June, 1950 because of recurrence of the insulin resistance. An attempt at intravenous administration was accompanied by a severe hypotensive reaction with collapse thought to be anaphylactic in nature. Erythema, wheal formation and induration were noted about the sites of insulin injection. Skin tests with all types of insulin produced a wheal and flare not seen in control subjects. Despite doses of insulin up to 1000 units daily, he developed severe acidosis requiring the intravenous administration of sodium bicarbonate. For several weeks he received 3000 to 6000 units of insulin daily until August during which time he received 50 mgm. of ACTH daily. On the fifth day of ACTH therapy hypoglycemic attacks developed and for the next three weeks there was no doubt of the im-

provement of ease in management of his diabetic state. Within a few days of stopping ACTH his insulin requirement again rose and even on 3000 units daily the fasting blood sugar ranged from 350 to 600 mgm.%, with a glycosuria of 50 to 100 gms. daily. The patient was then given a fixed diet and placed on constant insulin dosage of 600 units daily. For the first five days hyperglycemia and glycosuria increased, and he lost 8 pounds in weight. On September 23, ACTH 100 mgm. daily was begun. Weight loss promptly ceased and on the fifth day of treatment the blood sugar began to fall and glycosuria to lessen. On the eighth day insulin was reduced to 100 units because the blood sugar levels were normal and on the eleventh day was withdrawn completely. ACTH was continued until October 13 at 100 mgm. daily when it was discontinued abruptly. During the period of ACTH administration without insulin, hyperglycemia and glycosuria returned in moderate degree. On withdrawal of ACTH the fasting blood sugar promptly fell, ranging from 80 to 125 mgm. Since that time he has remained on a diet without insulin and periodic determinations of fasting blood sugar have all been within normal range. On November 12th he was given a test period of 5 days of 100 mgm. of ACTH. On day 4 the fasting blood sugar had risen to 200 and there was well marked glycosuria. Two days after cessation of ACTH the sugar level was again normal and there has been no subsequent glycosuria. Previous experience with the administration of ACTH to diabetic patients has shown that hyperglycemia and glycosuria are increased. In this case it seems possible that ACTH was of benefit through alteration of a hypersensitivity to insulin which seems to have been present as judged by the anaphylactoid reaction to intravenous insulin, the skin tests, and local responses at injection sites. When insulin was withdrawn the patient had about the expected degree of hyperglycemia and glycosuria in a mild diabetic under ACTH. Thus, it seems that two effects of ACTH were exhibited: one in overcoming a hypersensitivity reaction to injected insulin which blocked its physiological effect, and the other its usual diabetogenic action as an antagonist to the pharmacological action of insulin.

One of the most dramatic and interesting effects of ACTH and cortisone has been in the relief for varying periods of time of patients with bronchial asthma. Our studies conducted over the past 17 months have been in patients with chronic intractable asthma who had been able to secure no relief from any other type of treatment including symptomatic measures and desensitization. This represents the most serious type of problem for the allergist, and for the investigator the most reliable type of subject in which to study immediate response to treatment and duration of remission under a variety of treatment programs. The results to be presented tonight are as yet incomplete and this progress report is to be considered as purely preliminary in nature. The methods used in following these patients have been described previously.

TABLE 1

NUMBER OF PATIENTS WITH BRONCHIAL ASTHMA RECEIVING SINGLE AND MULTIPLE COURSES OF ACTH OR CORTISONE

PREPARATION	COURSES PER PATIENT	NUMBER OF PATIENTS
ACTH	One	34
	Two	8
	Three	6
	Four	2
	Five	3
	Six	1
Total		54
Cortisone	One	4
	Two	1
Total		5

As seen in *Table 1*, 54 patients have been treated with ACTH, one having received as many as six courses. The experience with cortisone has been less, but in adequate doses the response has been as satisfactory. In *Table 2*

is shown the degree of improvement in patients during their first course of ACTH or cortisone. It should be pointed out that all patients were given a predetermined dosage schedule and in some who did not receive complete relief the amount of drug administered was small and the eosinophil response not adequate. Noticeable improvement, both subjective and objective, was noted frequently within four hours and usually within thirty-six hours. In some instances, adjuvant therapy was no longer needed after a few hours; in others such medication could not be comfortably abandoned for a week or more. The time required to attain maximum benefit during the first course of ACTH or cortisone is shown in *Table 3*. Early improvement did not indicate eventual freedom from asthma, nor did the time to attain complete freedom forecast the duration of the remission. The patients who obtained complete relief during ACTH administration have been carefully followed to determine the length of their freedom from symptoms. The data is presented in *Table 4*. There is a very wide spread and as many of the patients are still in remission no final estimations are possible. As stated previously, 20 patients have received multiple courses of ACTH. Eleven of these have received at least two comparable courses of aqueous porcine material and a total of 14 comparable courses in the same patient have been administered. The results are summarized in *Table 5*. It is of interest that all had a complete response to the second course and that the duration of remission is slightly longer on the average after the second course. All patients who had received multiple courses have had a good initial response to each, including one patient who has been treated on six separate occasions. As a preliminary step to see if the dosage schedule which the patient had might influence the completeness and duration of his response, a comparison was made of the five patients with the longest and the five with the shortest remission (*Table 6*). All

TABLE 2

Degree of Improvement in Patients with Bronchial Asthma during First Course of ACTH or Cortisone

Preparation	Number of Patients	Patients Deriving Varying Improvement				
		Complete	Great	Moderate	Little	None
Porcine ACTH	45	36	5	4		
Long-acting porcine ACTH	4	4				
Bovine ACTH	1		1			
Total ACTH	50	40	6	4		
Cortisone	4	1		1	2	
Total ACTH and Cortisone	54	41	6	5	2	0

TABLE 3

Time to Attain Maximum Benefit during First Course of ACTH or Cortisone in Patients with Bronchial Asthma

Preparation	Number of Patients	Time to Attain Maximum Benefit	
		Average	Range
		days	*days*
Porcine ACTH	45	4.9	1–14
Long-acting porcine ACTH	4	4.5	3–6
Bovine ACTH	1	2	—
Total ACTH	50	4.8	1–14
Cortisone	4	6.3	5–7
Total ACTH and Cortisone	54	4.9	1–14

had complete relief of symptoms and in about the same period of time. However, the duration of the relief was greatly different in the two groups. It is seen that the total dose of ACTH was almost twice as great in the group with long remission and treatment was continued over 14 as compared to 6 days. These and other results suggest that there may be an optimal dosage schedule and an optimal duration of treatment which certainly may vary from patient to patient and which still remains to be determined. Before leaving the problem of bronchial asthma it seems worthwhile to touch briefly on two more points. One great difficulty with ACTH therapy has been the necessity for administration every six hours. For several months trials with a repository form of ACTH have been carried out. Depending on the severity of the disease it has been possible to obtain very satisfactory clinical results with one or two doses daily. The second point is so-called maintenance therapy. Even when carried out at very frequent intervals this has not appeared to appreciably prolong the period of remission.

During the course of these clinical studies as many patients as possible were followed closely by Dr. John Bordley of the Department of Otolaryngology. The techniques available permit direct observation of alterations in the mucous membranes and lymphoid tissue and material for microscopic examination can be obtained. The most interesting were those patients suffering from respiratory allergy. With adequate dosage of either ACTH or cortisone there was always a reduction in size and usually disappearance of nasal polyps. There was first of all a thickening of the mucous membranes of the polyp, and the translucent appearance changed to a delicate pink. Simultaneously, the nasal mucosa developed a deeper color, polypoid changes regressed, and the nasal discharge lessened. The polyps reappeared in all patients within two months. Comparative x-rays, before and after treatment, showed disappearance of polyps from the sinuses and much thinning of the lining mucous membranes. There seemed to be a definite correlation between the color changes in the mucous membranes and the development of eosinopenia. Similar changes were noted with the local application of cortisone. Disappointing were the changes noted in the lymphoid tissue in the nasopharynx. This tissue became an orange pink and could easily be distinguished from the

TABLE 4

Duration of Complete Remissions from First Course of ACTH or Cortisone in Patients with Bronchial Asthma[1]

Preparation	Number of Patients	Duration of Freedom		
		Average	Median	Range
		days	*days*	*days*
Porcine ACTH	32	65+[2]	54+	3–293+
Long-acting porcine ACTH	4	21+[3]	19+	4–42+
Bovine ACTH		(recent administration)		
Total ACTH	36	60+	48+	3–293+
Cortisone	1	60	—	—
Total ACTH and Cortisone	37	60+	48+	3–293+

[1] Excludes patients whose remissions began within the past 30 days.

[2] (+) denotes that some patients in the group are still in remission. Consequently, these values are also a function of the period of observation and tend to underestimate the length of remission.

[3] Because the long-acting ACTH is a more recent preparation, comparison with remissions obtained from regular ACTH is not possible.

TABLE 5

Pairs of Comparable Courses of Aqueous Porcine ACTH in the Same Patient with Bronchial Asthma (Summary Data)

Average Values	First Courses	Second Courses
Number of Complete Remissions	12	14
Time to Attain Maximal Benefit (days)	6.6	7.5
Duration of Remission (days)	40.2	46.5+
Eosinophil Count		
Before Treatment (per mm³)	1028	753
Per cent Fall	90	94
Days for Maximal Fall	4.0	5.8

surrounding mucous membranes. Cloudy or mucopurulent discharges were replaced by a layer of clear mucous, the crypts became more prominent and appeared clean. In general, however, there was no appreciable diminution in the volume of the lymphoid tissue present.

There can be no question of the efficacy of both ACTH and cortisone in controlling the active manifestations of disseminated lupus erythematosus. In essentially every case which has received adequate amounts of these hormones there has been a prompt and dramatic improvement in the general systemic manifestations with defervescence, subsidence of joint manifestations, and rapid improvement in most of the other clinical features. There is not yet evidence enough to finally evaluate the effect on cerebral and renal dysfunction, but the results thus far are rather discouraging. In several of the cases treated a phenomenon of interest has been observed which may have its counterpart in the course of treating other diseases with these hormones. When the dose of ACTH was reduced below 40 mgm. per day a temporary relapse often occurred which subsided spontaneously in each instance and has been designated the rebound phenomenon. It was characterized by a rise in temperature reaching 104 in some instances and gradually subsiding over a period of from seven to fourteen days. This febrile episode may be accompanied by a return of arthritis. This type of reaction is of some practical interest as it may not be necessary to resume treatment immediately if signs of activity appear toward the end of a given course of therapy.

TABLE 6

Five Longest and Five Shortest Remissions[1] in Patients with Bronchial Asthma Given Aqueous Porcine ACTH

Case	Remission			ACTH			Eosinophils		
	Per Cent	On Day	Duration (Days)	Total (Mgm.)	Starting dose (Mgm.)	Days	Before Therapy	Per Cent fall	On Day
Longest Remissions									
E. M.	100	7	293	732	20	21	484	97	5
M. G.	100	8	240	600	100	10	1496	100	2
B. M.	100	3	116	570	100	10	286	100	2
R. M.	100	2	108+[2]	430	40	14	206	89	1
K. W.	100	4	106+	595	50	16	187	100	7
Average	100	4.8	172+	585	62	14.2	532	97	3.4
Shortest Remissions									
B. deS.	100	3	3	285	85	4	858	91	4
B. deS.	100	3	3	210	40	5¼	1331	88	3
O. Z.	100	5	7	193	25	11	1056	92	4
S. S.	100	6	8	600	200	5	946	100	2
R. M.	100	4	11	200	40	5	1056	100	3
Average	100	4.4	6.4	298	78	6	1049	94	3.2

[1] Remissions in those patients obtaining complete relief.

[2] (+) denotes that patient is still in remission.

After the initial successes in the alleviation of certain manifestations of drug hypersensitivity, bronchial asthma, and nasal allergy by ACTH and cortisone interest was directed toward certain diseases of the eye in which hypersensitivity supposedly plays a part. The

eye, just as the nasopharynx, enables one to make direct visual observations of the tissue changes taking place. Striking improvement resulted in cases of non-granulomatous iritis, sympathetic ophthalmia, tuberculous uveitis, and vernal conjunctivitis. When the disease process was in the anterior portion of the eye the local application of cortisone was as effective as the parenteral administration of either ACTH or cortisone. The most striking effect of these hormones has been in the prompt control of the inflammatory and exudative phases of these various diseases of the conjunctiva and uveal tract. With parenteral treatment there is observed uniformly a subsidence of pericorneal congestion, clearing of the vitreous, diminution of exudates which become more circumscribed, and disappearance of retinal edema. In each instance there has been a concomitant improvement in vision. In each of the various types of disease which this group set out to treat there was reason to suspect an allergic factor in the inflammatory reaction. Non-granulomatous iritis is believed to be a phenomenon of bacterial hypersensitivity; in ocular tuberculosis the inflammatory phase depends upon a sensitivity of the tissues to tuberculo-protein; and there is evidence that the pathogenesis of sympathetic ophthalmia may be a sensitivity to the patient's own uveal tract pigment. It was a logical step to study these effects in the experimental animal where many of these ocular phenomena can be faithfully reproduced, and I would next like to present to you some work which has been performed by Dr. Alan Woods and Dr. Ronald M. Wood of the Wilmer Institute.

The first experimental attack was on the effect of ACTH and cortisone on certain well defined ocular allergic reactions in the rabbit including the ophthalmic reaction to protein agents, the bacterial allergic reaction and the focal reaction produced in tuberculous eyes by the systemic injection of tuberculin.

Nicolle and Abt first demonstrated that when guinea pigs were sensitized by the intraperitoneal injection of foreign serum and then given an anterior chamber injection of horse serum a violent ocular reaction with conjunctivitis, iritis, and hypopyon resulted. In the present experiments a series of rabbits were sensitized to horse serum by repeated intravenous injection. After demonstration that they were suitably sensitized and that a small amount of horse serum injected into the anterior chamber produced the characteristic reaction, the remaining animals were divided into three groups—one served as controls, the second were treated with 2.5 mgm. of ACTH every 6 hours for 48 hours prior to inoculation, and the third group with 10 mgm. of cortisone daily for four days before inoculation. After the anterior chamber inoculation all of the control animals showed marked ophthalmic reactions coming on after 24 hours and persisting for 11 days. There was essentially complete blocking of this reaction by ACTH and complete blocking in the cortisone treated rabbit.

The bacterial allergic reaction in the eye was first described by Derick and Swift. These investigators found that a marked tuberculin-like hypersensitiveness could be produced in animals by repeated intracutaneous injections of living alpha streptococci or by killed beta streptococci, and when the cornea of these animals was later scarified and a drop of specific bacterial antigen instilled in the eye, an ocular inflammation, characterized by a transient kerato-iritis developed after 24 hours.

Rabbits were sensitized by the repeated intracutaneous injection of a killed washed 18 hour culture of a group A-Beta hemolytic streptococcus suspended in normal salt solution. Two weeks after the last injection all animals gave well-marked skin reactions to the specific bacterial antigen. Anterior chamber injection of a suspension of killed organisms produced a well-marked iritis in these animals and no reaction in the normal rabbit. Three groups of sensitized rabbits were prepared as in the previous experiment—one as control, and the others treated with ACTH and cortisone prior to the ocular injection. The reaction was completely blocked in the cortisone treated animals. Similar suppression of the inflam-

matory reaction was noted in the ACTH treated animals. One month after cessation of treatment with cortisone and ACTH both control and treated animals were given a second anterior chamber injection. All animals then showed equal and marked ophthalmic reactions.

The focal reaction produced in tuberculous eyes by the systemic injection of excessive amounts of tuberculin has long been recognized clinically. In the course of a study of the effect of desensitization with tuberculin in experimental ocular tuberculosis, it was found that when immune-allergic rabbits with an early secondary ocular tuberculosis were given a shocking injection of tuberculin systemically, the diseased eye responded in 24 hours with a violent inflammatory reaction. Under these conditions even large doses of tuberculin produced no systemic manifestations.

A series of normal rabbits was inoculated subcutaneously with a small amount of a six weeks culture of human tubercle bacilli. All animals ran an asymptomatic course and six weeks later all showed cutaneous hypersensitivity to PPD. Three weeks later all animals received an anterior chamber injection of a small number of tubercle bacilli in the right eye. Three weeks later all showed early evidence of a secondary ocular tuberculosis with slight pericorneal congestion and minute tubercles in the iris. The rabbits were then divided into the same three groups as previously.

The violent inflammatory reaction seen in the control animal with pericorneal congestion, marked inflammatory changes in the iris and clouding of the cornea with increase in vascularization was absent in the cortisone treated animal. There was no increase in the inflammation after the injection of tuberculin. An interesting phenomenon was noted in the animals kept on cortisone. All evidences of inflammatory reaction disappeared from the tuberculous eyes. The tubercles in the iris, however, continued to increase in size and numbers presenting the picture of progressive nodular tuberculosis in the eye devoid of the usual inflammatory reaction.

It seemed quite clear in these experiments that ACTH and cortisone have the ability to block the inflammatory phase of the allergic reaction. The next question was whether this effect was confined to the type of inflammation associated with the hypersensitivity reaction or whether it was similarly manifested in inflammation not related to allergy. This point has been investigated by determining the ability of these substances to block inflammation secondary to certain irritants.

It has been clearly demonstrated that the injection of cortisone 10 mgm. daily for four days prior to anterior chamber injection and for five days afterwards completely blocked the inflammatory reaction to the introduction of glycerin into the eye.

It has long been known that an infusion of jequirity seeds instilled in the conjunctival sac produces a violent conjunctivitis characterized by congestion, chemosis and a mucopurulent discharge. In fact, many years ago, this was a fairly fashionable form of treatment for trachoma.

The systemic administration of cortisone or ACTH successfully blocked this type of inflammatory reaction. It is interesting to note that when the cortisone was discontinued a mild inflammatory reaction developed which subsequently paralleled that in the control animals.

These experiments confirm the clinical observations that ACTH and cortisone have a profound effect on certain ocular inflammatory and exudative reactions. It seems quite clear that both ACTH and Cortisone administered parenterally can block the inflammatory and exudative phase of the anaphylactic protein reaction in the eye, as well as that of the allergic reaction due to bacterial hypersensitivity, and of the focal reaction produced in tuberculous eyes by the systemic injection of tuberculin, this latter being another example of bacterial allergy. The first and most natural assumption is that in some way these agents

inhibit or influence the antigen-antibody reaction. The experiment showing that ACTH and cortisone block the inflammatory reaction due to irritants equally as well as they block the inflammation secondary to the hypersensitive reaction, is evidence that their action in blocking inflammation is not confined to those situations in which an antigen-antibody reaction plays a role.

As the final part of this lecture I would like to review with you some work which has recently been carried out in the Department of Pathology. Since our work had been stimulated by the studies of Rich and his coworkers in which it was shown that anatomical lesions similar to those seen in the collagen-vascular group of diseases could be produced in rabbits by anaphylactic hypersensitivity, it was of interest to see whether these lesions could be prevented by the administration of ACTH and cortisone. Rich and his colleagues have now performed three separate experiments comprising a total of 118 animals all sensitized with horse serum in the same manner and half of them treated with either ACTH or cortisone. Of the 59 control animals 51 or 86.4% developed endocarditis, periarteritis nodosa or both while such lesions were found in only 23.6% of the animals treated with one of these hormones. This is of interest in relation to the healing of active periarteritis nodosa in the human subject which takes place during the administration of ACTH and cortisone.

The more recent work of Rich and his coworkers in relation to the type of experimental nephritis which develops as a result of hypersensitivity is of even more interest (7). They have shown that a glomerulonephritis, having all of the pathological characteristics of human glomerulonephritis, can result from anaphylactic hypersensitivity. Nephritis of varying degrees of severity occurred in 61% of the untreated, sensitized animals, while only 15% of the ACTH-treated animals developed any glomerular lesions. As noted above cortisone suppressed the development of periarteritis nodosa and cardiac lesions with about the same efficacy as ACTH, and it was even more efficacious in preventing the endothelial proliferation characteristic of glomerulonephritis. Nephritis occurred in 51% of the untreated sensitized animals, but in none of the cortisone-treated animals was there any increased cellularity of the glomerular tufts. However, it was found that in 71% of the cortisone-treated animals many of the glomeruli showed serious alterations of a type quite different from those of ordinary glomerulonephritis. These alterations consisted in focal, aneurysmal-like dilatations of glomerular capillaries, with rupture and hemorrhage, or hyalinization of the contained blood or inspissated plasma, producing homogeneous masses in the tufts. As a result of the increased frequency of rupture of tuft capillaries, there was much more blood in the tubules than even in the untreated controls with proliferative glomerulonephritis. The hyalinized masses in the tufts of the cortisone-treated animals may resemble the isolated, globular, hyalinized masses that occur in the glomeruli in diabetics—the Kimmelstiel-Wilson lesion. Evidence indicates that cortisone alone, in the absence of hypersensitivity, may cause glomerular lesions of this type. Why these lesions have occurred in the cortisone-treated animals and not in those treated with ACTH is not clear. It may be a result of dosage.

As to the application of these observations to the therapy of human glomerulonephritis with ACTH and cortisone it would seem reasonable to expect that since these hormones do inhibit anaphylactic vascular injury in other tissues in man as in the experimental animal, they will likewise inhibit the injury to the glomerular capillaries. The present experiments deal with prevention of damage and it is obvious that destroyed glomeruli or organized portions of glomeruli cannot be restored. In most of the cases of human nephritis so far reported, in which these hormones have been tried therapeutically, treatment was not begun until at least several weeks after clinical manifestations of renal injury had become evident.

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Topectomy, 1946–1951—Report on 106 Consecutive Non-project Topectomy Operations*

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MORE than 4 years having elapsed since the first topectomy was done in October 1946 (1), (1a), an appraisal of the operation seems in order, especially with regard to the site, amount and technical aspects of this type of bi-frontal cortical ablation. The following communication, therefore, will stress primarily the neurosurgical aspects of the operation in this consecutive series of 99 "non-project" patients, representing 106 topectomy operations. The term "non-project" is used to designate those patients not included in various state hospital projects already described (2) or about to be reported (3), (4).

Topectomy (from the Greek topos, place, and ektome, a cutting out) (2) refers in the following discussion to the symmetrical surgical removal of a segment of cerebral cortex from the forward part of each frontal lobe of the brain for the treatment of mental illnesses or for intractable pain. It is an operation that was devised and subsequently modified in the effort to develop a procedure more selective as to operative site and more conservative as to the amount of brain tissue disconnected than the standard frontal lobotomy or leucotomy. Penfield expressed much the same idea with reference to gyrectomy, a procedure similar in certain respects to topectomy, by saying: "It seemed desirable to seek a procedure which might have the same therapeutic effect as [lobotomy], and yet preserve the function of more of the frontal cortex." (5)

The first recorded use of brain surgery for the treatment of mental illness actually consisted of removal or ablation of cerebral cortex as reported by Burckhardt in 1891 (6), (10). Then in 1935–1937 Egaz Moniz introduced the procedure known as frontal leucotomy (7) for which he has recently been awarded a Nobel Prize. Subsequently Freeman and Watts (8), Lyerly (9), Poppen (10) and many others have modified this procedure, which in this country became known as frontal or prefrontal lobotomy.

Whereas lobotomy may be defined as surgical section of nerve fibers connecting the surface gray matter or cortex of the frontal lobes with more remote and deeper portions of the brain, topectomy means the removal, ablation or cutting out of only a fraction (generally about 50% or less) of the cortex or surface gray matter that would be disconnected and thereby isolated by a standard prefrontal lobotomy. In essence, therefore, topectomy is a surface operation which thus enables the surgeon to gauge more accurately and precisely what part of the brain he is operating upon and how extensive an operation he is doing, in contrast to lobotomy which is a sub-surface operation that has occasionally eventuated in fatal hemorrhage (8), (10) or unexpectedly wide variations in the placement and extent of its cuts deep in the brain substance (11), (12).

Selection of patients: The selection of patients for topectomy follows essentially the same criteria as those for frontal or prefrontal lobotomy or leucotomy (8), (10), briefly summarized by Tucker and Dynes (13) as follows: "(1) There should be symptoms of agitation, depression or self-concern; (2) the condition (i.e., the mental disease) should be such that it could not be expected to respond to any other type of treatment; (3) the degree of

* Nathan Lewis Hatfield Lecture XXXV, The College of Physicians of Philadelphia, 4 April 1951.

suffering and incapacity must be sufficient to justify the operation; (4) the family situation should be favorable for rehabilitation of the patient; (5) the expected post-operative condition must be considered a sufficient improvement to justify the operation; and (6) there should not be organic brain disease."

Munro adds (14): "There seems to be general agreement that the clinical conditions that are apt to respond favorably to one or another of the various types of proposed operations are chronic agitated depressions, varieties of schizophrenia with a large emotional or paranoid element, chronic obsessive-compulsive neuroses,—", etc.

However, one must also be aware of the possibility so well expressed by Murphy (14a) with regard, for example, to brain surgery for the patient with an obsessive tension state, to the effect that operation has produced some "brilliant therapeutic successes but also many of the most annoying and trouble-making failures in the whole group of psychiatric patients treated surgically—it must be added that in this type of mental illness lobotomy may prove to be the proverbial two-edged sword. The self-effacing, correct, polite, obsessive-compulsive individual may, like the souvenir hand-grenade, blow up in the faces of all concerned when tampered with, to the consternation and persistent disappointment of physician, family and society. What is meant by 'failure' in this group is that the patient's behavior can become so aggressive and exclusively self-concerned as to constitute psychopathy."

Of the schizophrenic group, which constitutes the majority of patients recommended for topectomy, the pseudoneurotic type (33) may be expected to respond the most favorably and the predominately paranoid type of older age group (30–34 years of age) the next best, especially when there is at least some manifestation of a desire to get well. The results in the younger group (20 to 25 years) and in the chronic badly deteriorated category, especially of the catatonic or hebephrenic classifications, are poorer, and at best are generally only palliative.

Best results following topectomy in the non-schizophrenic group may be expected in depressed cases of the agitated, involutional or reactive type who have not shown sustained benefit as the result of psychotherapy and shock treatment. As a rule obsessive tension states also respond well to topectomy.

Topectomy for the relief of pain due to cancer is not usually recommended because for persons debilitated by a malignant disease it is an operation of somewhat greater surgical magnitude than lobotomy. However, as pointed out elsewhere, various risks of lobotomy may in other respects make lobotomy a potentially more hazardous procedure. The two cases in this series on whom bifrontal "9–10" topectomy (see below) was done for alleviation of pain due to carcinoma experienced gratifying relief. LeBeau (15), Tinsley (44) and others (16) have also found topectomy satisfactory for relief of intractable pain, and one case has done well as to pain relief, for more than six months, following a unilateral 40 gm. area "9–10" topectomy (16a).

The author and his psychiatrist colleagues at present feel that no brain operation for the treatment of mental or emotional illness should be done unless the patient has been seriously and overtly ill for at least two years, so that in most cases of this series the illness has clearly been present for at least 6 years and in several cases for as long as 18 years. The duration of the illness and the age of the patient however do not of themselves necessarily preclude a good prognosis after topectomy, except in older chronically deteriorated schizophrenics for whom the prognosis is poor.

Indeed, since schizophrenic patients who are markedly "deteriorated" seldom show lasting improvement after topectomy (33), a more extensive operation such as lobotomy is recommended for them initially if a palliative procedure is desired, after which they may become more manageable.

In all cases on whom the writer has done a topectomy for the treatment of mental illness, the operation has been recommended by one or more competent psychiatrists, and only after

an adequate trial of psychotherapy and also shock therapy when the latter is indicated. This is a rule urged upon all neurosurgeons engaged in the practice of "psycho-surgery", to use the term employed by Freeman and Watts (8).

Preoperative examination: In addition to evaluation by the psychiatrist every patient prior to topectomy is submitted to a physical and neurological examination, a complete blood count, blood Wassermann or Mazzini test, urinalysis and whenever feasible, x-rays of the skull, an electroencephalogram (EEG) and psychometric tests. In special instances other tests may also be indicated.

OPERATIVE TECHNIQUE

Anesthesia: With the exception of two cases operated upon under local novocain anesthesia, all topectomies in this series were carried out under general anesthesia using 1.5 to 3.5 gms. of intravenously administered sodium pentothal supplemented by oxygen-nitrous oxide via intratracheal intubation (17). Preoperative medication usually consisted of morphine sulphate 0.015 gms. and scopolamine 0.0004 gms. by hypodermic.

Operative exposure: Scalp incisions were planned with every regard for subsequent cosmetic effects and were, therefore, usually placed so as to be concealed by the hair. This generally entailed the use of a generous curved trans-coronal incision permitting forward reflection of an anterior scalp flap on the supra-orbital ridge (*Figure 1*). In women, it has not been found necessary to shave the hair from the posterior half of the head.

In earlier cases exposure of each frontal lobe was achieved by turning two separate bone flaps. In some of these cases a midline bridge of bone was left over the superior longitudinal sinus; in others the bone flaps were bi-valved by making a single saw cut along the midline. In most later cases, however, a single transfrontal bone flap hinged on the right temporal muscle was used. Midline as well as corner trephine or burr openings are advisable for this type of flap (*Figure 1*). In a few cases, when the frontal air sinuses were large and, therefore, necessarily entered, the sinus opening after exenteration of the sinus mucosa was packed with a muscle or Gelfoam stamp saturated in penicillin solution. No complications or infections occurred as a result of this. Indeed, the chief technical difficulty encountered in the use of the single transfrontal bone flap was an occasional small rent in the dura at the extreme anterior aspect of the flap which occurred usually in female patients between 60 and 70 years of age, with thin adherent dura at this site. Because of this a number of later topectomies, especially in older patients, were carried out through large ($1\frac{3}{4}$ inch) bilateral crown-trephine openings.

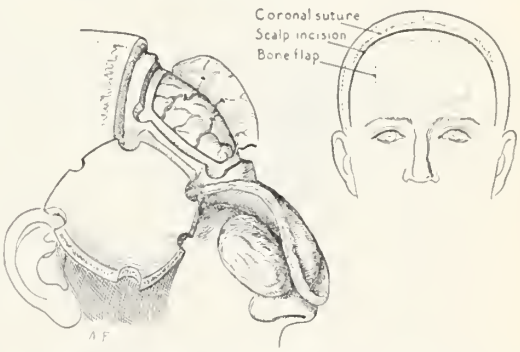

Fig. 1. Operative Exposure for Rostro-Medial "9–10" Type of Topectomy.

In all cases dural bleeding points over and adjacent to the superior longitudinal sinus were carefully controlled by the electrocautery. As an added precaution permanent dural stay sutures were used when necessary to hold the dura up against the bone edges while Hemopak (Johnson and Johnson) or Gelfoam (Upjohn) was employed where indicated. A right and left dural flap hinged along the midline was then reflected to expose each frontal lobe, care being taken to avoid tearing any of the superior cerebral or frontal veins between the cortex and dura by preliminary cauterization or clipping of these veins prior to their division. The rostro-dorsal aspect of each frontal lobe could thus be well exposed as far medially as the falx cerebri.

Gross pathology: In studying the gross appearance of the brain as thus exposed it was noted that excessive amounts of cerebrospinal fluid, thickened arachnoid and/or an unusual degree of cortical atrophy was apparent in varying degrees in nearly half of these cases, especially those of the long-standing schizophrenic group and in the one "juvenile schizophrenic" operated upon. Yet microscopically, analysis of excised cortex failed to show any consistent abnormalities in these or in other similar patients (2).

Operative site: The site for cortical ablation was always determined as carefully as possible

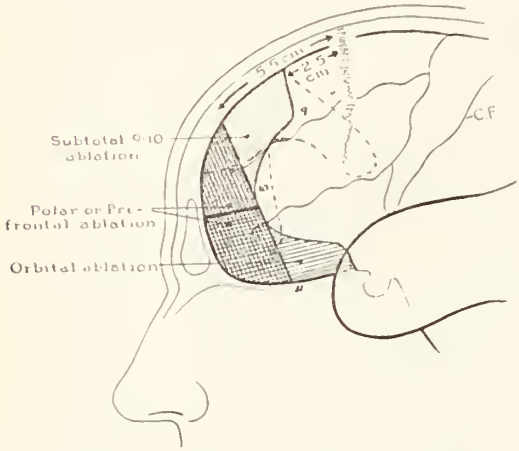

Fig. 2. Diagram of Various Types of Topectomy. Approximate Extent of Brodmann's Areas 9, 10, and 11 Indicated by Dotted Lines.

by reference to fixed landmarks such as major cerebral sulci, the falx cerebri, frontal poles, sphenoid ridges, olfactory tracts and coronal and sagittal sutures, as dictated by the requirements of each case. Because of the known variability of structures such as the cerebral sulci and coronal sutures (18), (45), it was often desirable to check the site for resection with reference to the motor cortex (4) or cingulate gyri (19), (37), since these could be identified by the regular techniques of electrical stimulation described by Penfield, (20), (21) and others. It was felt, too, that this might be of great value for the future treatment of each patient if a subsequent operation should prove necessary, as proved to be the case in several instances.

The location and amount of cortical ablation was purposely varied in sub-series of this group of patients during the four year period under discussion, according to the dictates of experience and study. In the earliest cases every effort was made to confine the ablation to the more rostral portion of each frontal lobe for reasons given elsewhere (1). Next, efforts were made to confine removals grossly to the region of area 9 of Brodmann (1a). (Since it is realized that the cytoarchitectonic areas of Brodmann (22) obviously cannot be localized accurately, any references to these areas in this text will refer only to *an estimation* of their sites.) Later still it seemed to some of us that better results in psychotic patients followed ablations from the rostro-medial portion of each frontal lobe representing, it is believed, the medial parts of areas 9 and 10 of Brodmann (1a). For a while, therefore, this type of ablation was done. Each resection of this kind measured approximately 5.0 x 3.5 x 1.9 cm and was begun 2.0 to 2.5 cm anterior to the coronal suture at the midline (17). For convenience this will be referred to hereinafter as an area "9–10" topectomy.

In the past two years, as the result of observations on a series of topectomies in a New York State project (4), cortical ablations have been carried out in an oblique plane combining the rostro-ventral part of the "9–10" topectomy with resection of the rostral half of the orbital gyri. The plane of this prefrontal resection begins 5.0 to 5.5 cm anterior to the point where the coronal suture crosses the midline and terminates on the orbital or ventral aspect of each frontal lobe approximately halfway between the frontal pole and the optic chiasm (*Figure 2*), with the idea of leaving intact much of the dysgranular cortex described by Beck (23) and referred to by Pribram (24) *et al.* The hope was also entertained that the risk of postoperative seizures would thereby be minimized, not only because this prefrontal or polar type of resection was carried out at a greater distance from the primary

motor cortex but also because fewer superior cerebral veins need be divided, thus reducing the chance of remote venous thromboses that might lead to seizures. Thus this polar type of topectomy, so called because it includes total removal of the frontal poles, has currently become the procedure of choice. Presumably it is comprised of the bulk of area 10 and the rostral portion of area 11 (*Figure 2*).

Considerable controversy still exists as to the optimum site for frontal lobe surgery in the treatment of mental illness, as indicated in the 1951 Salmon Lectures by Professor John Fulton (25). However, the author's experience with this series of non-project patients together with certain state hospital project studies (2), (4) now suggests that it makes little difference as to clinical results whether cortical ablation is confined principally to the region of Brodmann's areas 9 and 10, or to the orbital surface of the frontal lobes (principally area 11) as in a state hospital series, (2), (4), (33), or to combinations of both, as in the polar "10–11" type of topectomy involving area 10 and the rostral portion of area 11. The latter type of operation is now preferred not only because the seizure incidence is less (*Table II*), but also because it avoids more caudal portions of the lateral and medial aspects of the frontal lobes where operative intervention, as in radical or "posterior" lobotomies, may occasionally produce an apathetic incontinent patient. (While deleterious effects following more caudal operations are probably due to the

TABLE I

FOLLOW–UP DATA

99 Cases 106 Topectomies

YEARS AFTER TOPECTOMY:	4	3	2 1/2	2	1	less than 1	no recent data	2nd topectomy
SCHIZOPHRENIC (No. of cases):	4	9	19	19	8	3	6	5
OTHERS (" " "):	1	5	3	4	9	8	1	2
TOTAL:	5	14	22	23	17	11	7	7

TABLE II

Single Asterisk (*) Indicates One Additional Patient With Less Than One Year Follow-up Had Seizures Following Operation. Double Asterisk (**) Indicates That Some of These Nine Patients Had Evidence Suggesting a Predisposing Convulsive Factor Prior to Topectomy (see text) and That Others Had No More Than Two Episodes.

SEIZURE INCIDENCE

81 Cases with 1-4 years follow-up

	AREA 9 ABLATION			SUBTOTAL 9-10 ABLATION			POLAR ABLATION			TOTAL		
	No. of cases	No. of Cases with seizures	%	No. of Cases	No. of Cases with seizures	%	No of Cases	No. of Cases with seizures	%	No of Cases	Cases with seizures	%
One Topectomy only	7	1	14	45	9**	20	8	0	0	60	10	16
Two Topectomies	0	0		7	1		0	0		7	1	
Topectomy after Lobotomy	1	1		1	1		0	0		2	2	
Lobotomy after Topectomy	1	0		3	0		1	1		5	1	
Topectomy after Transorbital Lobotomy	0	0		4	0		3	0		7	0	
TOTAL (incl. 2 Ops.)	9	2*	22	60	11	18	12	1	93	81	14	17

additional quantity of brain function thereby disconnected, some of these effects may be related to the more caudal site of the operation, as pointed out elsewhere (17).)

As to operations upon the rostral cingulate cortex, the first recorded bilateral cingulate ablation was described by the author as part of the first Columbia-Greystone Project of 1947 (2). Because little benefit followed this operation it was discarded. However, Hardman (26), Le Beau (27), Cairns (28), Livingston (29) and others have since done a number of anterior cingulate ablations and tentatively report some good results, especially in patients who are not chronic schizophrenics. McLardy and Meyer (46) however feel that isolation of anterior cingulate cortex by lobotomy is not of therapeutic value.

While the question of the optimum site for frontal lobe surgery therefore remains open, the author knows of no data clearly indicating that operative intervention at a given frontal lobe site leads to significantly better results than at another (33), (45), (46). For want of evidence to the contrary plus the advantages enumerated above, therefore, the bilateral prefrontal, polar or area 10 and rostral 11 type of ablation is currently the ablation of choice, (*Figure 2*), and has been for approximately two years.

Quantitative factor: The actual amount or quantity of cortex removed in any type of topectomy seems to be far more significant than the site of ablation. For example, since the aim of topectomy is to do the smallest possible operation upon the brain that might be expected to help the patient recommended for the procedure, efforts were made in 21 of our earlier cases to resect as small an amount of cortex from the rostro-medial aspect of each frontal lobe in the region of area 9 as seemed reasonable. Each block of resected cortex in these smaller ablations measured only 3.0 to 4.0 cm in length, 2.5 to 3.0 cm in width and 1.9 cm in depth, with an average weight of 20 gms apiece.

It soon became apparent however that while some non-schizophrenic patients with these small ablations improved (and to date 6 of the 8 in this category have maintained their improvement) 13 other patients did not improve (11 of the schizophrenic group, 1 obsessive-compulsive and 1 with involutional melancholia). A second topectomy operation was therefore performed several months later on 7 of this group of 13 failures, for removal of an equivalent amount of additional cortex (principally from the region of area 10) rostral to their initial topectomy. These seven topectomies which were at first essentially area 9 operations, were thus converted to subtotal "9–10" ablations and have been so listed in the appended tables of results. (The only failures after this second topectomy occurred in schizophrenic patients.) The fact that 4 of these 7 re-operated cases have shown lasting improvement after their second operation strongly suggests that the quantitative factor is an important consideration in such operations. This premise seems to be further substantiated by the fact that of 7 other patients who failed to improve after bilateral transorbital lobotomy and then had a topectomy of the "9–10" or the polar type, 3 have been greatly benefited by the subsequent topectomy.

It has also become apparent that regardless of an extensive two-stage combined procedure like cortical ablation plus lobotomy, improvement may not take place in some patients as illustrated by six schizophrenic cases in this series. Two were not benefited by a "9–10" or area 9 topectomy, respectively, carried out two years after bilateral prefrontal lobotomy had failed to help them. Conversely, lobotomy after topectomy in four other cases was followed by no appreciable change in three and profound apathy and early death in a fourth case, operated upon elsewhere for lobotomy.

A further indication that the *quantitative factor* is more important than the *site* of cortical ablation is afforded by a comparison between the weight or volume of the ablated tissue and post-operative clinical results. It has been found for example, in this and other series of topectomies, that removal of only 20–25 grams from each frontal lobe, whether from the region

of area 9 or more rostrally, is capable of reducing the response to the pain of cancer and thus "relieving" the pain without serious adverse effects on the personality or intellect. A more extensive procedure, however, such as bilateral prefrontal lobotomy in similar patients may induce severe personality and intellectual deficits.

It has also been found that removal of no more than 15–20 gms. from the region of area 9 or "9–10" is usually not sufficient to achieve lasting improvement in sufferers from the primarily affective group of psychoses or from psychoneuroses, whereas a second topectomy with removal of an additional 15 gms. from each frontal lobe has thus far led to enduring improvement in this category of cases. Most patients in these categories furthermore have shown significant improvement if their initial topectomy consisted of 30–35 gms. removal from each side regardless of whether a subtotal 9–10 procedure or the polar type of topectomy was done (*Table III*). Obviously therefore there has been no reason for carrying out a more radical procedure in such cases.

For the non-deteriorated schizophrenic experience has indicated that the minimal effective amount of cortex that should be removed from each frontal lobe in order to achieve significant post-operative improvement is 35–40 gms. For the chronic deteriorated schizophrenic, however, if ablation of 40–45 gms. from each side fails to induce a palliative effect, then a more radical procedure may also fail in about half of such a group. Krueger has had a similar experience (36).

These observations as to quantity therefore suggest that there is a critical value as to the amount of cortex that should be removed from each frontal lobe, depending on the condition for which the operation is recommended, as follows:

TABLE III

Asterisk (*) Indicates that Patients With No Recent Follow-up Have Been Included in This Group.

RESULTS AND TYPE OF ABLATION

(99 Cases)

	INSIGNIFICANT OR NO IMPROVEMENT*			SIGNIFICANT IMPROVEMENT			
	Area 9	9 & 10	Polar	Area 9	9 & 10	Polar	
SCHIZOPHRENIC (No. of Cases)	4	38	2 = 44	2	19	3 = 24	= 68
OTHERS:	2	2	6 = 10	6	10	5 = 21	= 31
TOTAL:	6	40	8 = 54	8	29	8 = 45	99

CONDITION	RANGE OF OPTIMUM AMOUNT OF CORTICAL REMOVAL	
	Unilateral (Grams)	Total of both sides (Grams)
Pain	20–25	40–50
Affective disorders	30–35	60–70
Schizophrenia—		
non-deteriorated	35–40	70–80
deteriorated	40–50+	80–90+

While the average values just listed are believed to represent a reasonably accurate picture of the quantitative factor in topectomy, certain sources of error must be considered. For example, a variable degree of tissue change obviously takes place around each cortical excision despite every effort to achieve uniform ablations in comparable cases. Secondly, in some of the earlier ablations, the weight or volume (the two for practical purposes being essentially identical for brain tissue) was estimated from dimensions of the operative cavity and/or the freshly resected block of cortex, instead of, as in later cases, by weighing the

freshly excised tissue or by determining its volume by the amount of water displaced by the specimen. Any additional tissue removed by suction line was included by collecting it in a special bottle in the suction line.

Some variations in the quantity of resected cortex were also purposely made according to the chronicity of the illness and the severity of psychotic behavior. Of two patients in the psychotic group for example, the one with the more chronic history and more severe behavior disturbances and greater degree of abnormal psychotic ideation usually had 40 rather than 35 gms. removed from each frontal lobe. Another factor influencing the amount and dimensions of cortical ablation was the size and appearance of each brain, for the removal of 30 gms. from an extremely atrophic or small brain might be the equivalent of 35 gms. from a more normal looking, or larger brain. Certain variations as to quantity were thus made in the effort to carry out the most effective type of procedure for each individual patient in later cases in this series.

Technique of ablation: The actual technique of cortical ablation has now been standardized after initial trials of different methods. First of all it is helpful to mark the boundaries of the proposed resection with a black thread laid on the surface of the brain (2). The cortical incisions are then planned as far as possible so as to leave a sulcus between the proposed incision and the adjacent intact cortex to serve as a barrier to the spread of post-operative gliosis.

The actual removal of cortex has been done by the exclusive use of fine silk ligatures; by the subpial technique; and by the exclusive use of silver clips without resort to the electrocautery, as well as by the electrocautery alone. Combinations of these techniques have also been used. However, there is an almost equal percentage of patients after each of these operative techniques who derived clinical improvement or who did not, or who suffered one or more post-operative seizures or who did not. These considerations, plus the longer time required by the exclusive use of the subpial, clip or silk ligature techniques, have led the writer to feel that sharp dissection combined with careful, restricted use of silver clips and the electrocautery at its minimal effective intensity was the most satisfactory method of cortical removal.

The superior cerebral veins over the designated area of cortex having been divided, the frontal lobe is gently retracted away from the falx so that the appropriate polar and frontopolar branches of the anterior cerebral artery can be secured on the medial aspect of the frontal lobe 1.9 cm ventral to the junction of its lateral or convex surface with its medial surface. Surface vessels elsewhere along the proposed line of excision having been secured with silver clips or the electrocautery, the desired block of cortex is cut away from the brain by sharp dissection with a No. 11 scalpel, held perpendicular to the surface of the brain. As the average depth of the frontal convolutions of gray matter is 1.9 cm, the blade is always marked off at this depth. The under surface of the block of cortex is then cut away at a depth no greater than 1.9 cm with a sharp spatula, and remaining bleeding points sealed with silver clips or the electrocautery. In some cases it may be necessary to remove some additional cortex with a small caliber suction tip to achieve the desired quantity or to trim the wound edges evenly. When the resultant cavity is completely dry, the anesthetist is asked to make the patient cough or "buck" so that the surgeon can check the effectiveness of venous hemostasis. The cavity is then lined with a thin filmy layer of oxidized cellulose (Hemopak) or Gelfoam and 5.0 cc of 1:1000 Penicillin solution (5,000 units) is instilled into each cavity. The dura is then carefully closed in water-tight fashion with black silk sutures. On replacing the bone flap its periosteum is approximated with interrupted black silk sutures while bone dust, bone buttons, tantalum discs (30), or small pieces of stainless steel mesh (31) are used to fill or cover the anterior burr holes. The scalp is then closed in layers in the usual manner. Drains are seldom used as they may constitute an avenue for wound in-

fection and are not always effective. Finally, a firm head bandage is applied.

At the conclusion of each operation the patient generally begins to awaken, move about and even talk while still in the operating room or very shortly after leaving it. Intravenous fluid administration is completed as indicated on the ward or in the room, 500 to 1,000 cc blood usually being given during each operation plus 500 to 1,000 cc of 5 per cent glucose in distilled water.

Re-operation: Re-operation for additional bilateral ablation of frontal cortex has been carried out in 7 cases several months after initial topectomy in much the same manner as the initial procedure. After re-elevation of the bone flap, however, generally only the anterior edge of the dural flap is re-opened lest adhesions between the dura and the rest of the previous operative site be disturbed (for light adhesions have always been found between the dura and the margins of the original operative cavity as might be expected). The cortex and white matter around the original operative site have usually appeared yellowish for a distance of 0.5 to 1.0 cm, where subsequent microscopic analysis shows astrocytosis and some cell loss. Yet electro-corticograms at re-operation in four cases so studied have shown no abnormalities (under sodium pentothal anesthesia) of the cortex surrounding such cavities even within this 0.5 to 1.0 cm zone.

Post-operative course: After recovery from the effects of anesthesia the immediate post-operative course is usually marked by a 24 hour period of improved behavior, often accompanied by euphoria. From the second to seventh post-operative day, however, marked regression from this initial state of improvement is usually manifest, often characterized by profound accentuation of pre-operative psychotic behavior, perhaps accompanied by extreme violence or negativism, incontinence, and sometimes masturbation. Within a week or so after operation fluctuating signs of improvement gradually become apparent especially in those patients who eventually are to show lasting improvement. Thereafter slower gains in behavior and attitude may occur for another six months or more, and during this period some patients at times may be slow to dress, eat or bathe, and may feel unduly fatigued. Convalescence in a mental hospital or at home is usually recommended for two months or so after operation, and, of course, continuation of psychotherapy.

Permanent incontinence of urine or feces has not occurred after topectomy, although the former has been transitory during the immediate post-operative period in about one third of these cases. Temporary post-operative atelectasis has occurred in two cases and transitory vitamin deficiency in one.

Post-operative hematomas, which occurred after three of these 106 operations, were promptly evacuated by re-elevation of the flap so that all three patients are now home and physically well. One has been working and travelling extensively for nearly 3 years while another has recently completed a transcontinental tour by himself. The only one of these three to suffer any post-operative seizures had an abnormal EEG before topectomy.

There have been no wound infections in this entire series and only one instance of paresis, caused by temporary anesthesia complications. The incidence of post-operative seizures will be discussed separately below.

There has not been a single operative death in the 106 topectomy operations as compared to a post-lobotomy mortality rate ranging from approximately 1 to 6%. Indeed, the author has now performed or guided nearly 300 bifrontal topectomy operations including those in various state hospital projects without a single operative death. (In two separate state hospital series, however, two patients were lost after other types of frontal lobe surgery (2), (3).)

Post-operative seizures: When seizures have occurred after topectomy they have almost invariably happened between the fourth and 13th post-operative month, while thus far only one has developed any convulsions if free of seizures for a year after topectomy, even when no anti-convulsant medication has been

taken. Indeed, the first five patients operated upon over four years ago have all been seizure-free although none have had anti-convulsant medication. This also applies to the next 14 patients making a total of 19 followed for three years or longer. For this reason, and also because anti-convulsant medication may affect the mental acuity, gait or gums, it was not prescribed for many of the earlier topectomy cases unless indicated. More recently, however, patients in this and other topectomy series have been given such medication as a precautionary measure for at least a year after operation.

Seizures have been generalized, with the exception of one patient who had two episodes of focal onset; and in most cases have been well controlled by phenobarbital or sodium dilantin. The few cases difficult to control have had evidence of pre-existing organic brain disease and/or considerable residual emotional tension. With one possible exception, however, none of these patients had been prevented from carrying on their usual work or activities because of their seizures.

In this series of 106 consecutive topectomy operations on 99 patients, seven patients have had a second topectomy and fourteen a topectomy plus some type of lobotomy. Eighteen of the 99 cases are omitted from this part of the discussion because for seven there is no recent follow-up data and for eleven others an insufficient post-operative follow-up interval (of less than 1 year) has elapsed. All of the remaining 81 cases have been followed for a year or more as follows: 17 for at least one year; an additional 45 for at least two years; 14 for three years and 5 for four years or more (*Table I*). Excluding for the moment the four who did not develop seizures until after the *second* brain operation (prefrontal lobotomy plus topectomy or two topectomies) there remain 77 patients with a follow-up of one to four years of whom 10 have had post-operative seizures, an incidence of 13%. (This compares favorably with the 12.3% seizure incidence after lobotomy (8) reported by Freeman and Watts.) However, based only on those cases with one topectomy, the seizure incidence is 16% (*Table II*). Four of these topectomy patients have had no more than two seizures apiece while six have had three or more. In three of these 10 cases moreover there was evidence of some predisposing seizure factor. One schizophrenic patient, for example, precipitated a convulsion by unauthorized self-administered insulin after operation; one almost died, before topectomy, of status epilepticus induced by electric shock therapy; and another patient admitted convulsions in childhood, had a "borderline" abnormal EEG before topectomy and sometimes failed to take the prescribed anti-convulsant medication after operation. Thus only seven (9%) of these 77 developed post-topectomy seizures without an apparent predisposing cause.

Four additional patients did not develop seizures until several months after the second operation. One of these had a second topectomy, two had a topectomy after a previous prefrontal lobotomy and one had a prefrontal lobotomy after a topectomy. None of seven other patients who had a transorbital lobotomy followed by topectomy have had any seizures. The four doubly operated patients with seizures plus the ten already mentioned make fourteen of 81 patients with a follow-up of over one year who developed post-operative seizures (18%). One additional patient (* in *Table II*) with postoperative seizures was followed only 8 months when she died of advanced Parkinson's Disease which had been accompanied by suicidal depression. This makes a total of 15 of 82 patients or 18% who developed seizures.

To recapitulate: When the incidence of convulsions after *two* operations upon the brain (lobotomy plus topectomy or two topectomies) is included, the total seizure incidence in this series amounts to 18%. However, when the four patients who developed seizures after a second operation are excluded, the total post-topectomy seizure incidence is 13%, while the incidence based only on cases with one topec-

tomy is 16%. Finally, for cases that were free of any predisposing factor the incidence is only 9%.

Discussion of seizures: A careful review of this and other series of topectomies reveals no correlation between the effect of variations in the surgical *technique* of cortical resection and the incidence of post-operative seizures. As to the possible effect of the *site* of cortical ablation on seizure incidence there seems to be some indication that the nearer the operative intervention is to the motor cortex, the higher may be the percentage of seizures. For example, the incidence of seizures is less after the more rostral polar type of topectomy than after the area 9, or the subtotal "9–10" type of resection and is far lower after removal of the orbital gyri (4) than after equivalent amounts of cortical ablation from the region of Brodmann's areas 9 and 10. The seizure incidence, moreover, was even higher in the first Columbia-Greystone series (2) in which several cortical removals were carried out close to the motor cortex.

It is possible that two pathological mechanisms are operative in the production of post-operative seizures after topectomy. One is the obvious factor of gliosis at the actual site of any brain operation. For example, seizure incidences even after lobotomy may range to 18% (15a) and even 33% (32) with an average of approximately 10 to 12% (8), (10), (10a).

It is also possible that remote pathological changes in the cortex close to the motor cortex may be occasioned by alterations in cerebral circulation and/or gliosis secondary to ligation of anterior superior cerebral veins, especially as it is known that ligation of these veins may, without actual surgery upon the brain itself, lead to seizures (3). Indeed, the lower incidence of seizures after the rostral (polar) topectomies of this series and after the orbital ablations of another series (4) may reflect the fact that they required less extensive ligation of major cerebral veins.

Another factor that seems to have some influence, but not an exclusive bearing on seizure frequency is the degree of post-operative tension or hostility that may still be harbored by the patient, for the greater it is, the more prone certain individuals seem to be to seizures despite appropriate medication. Finally it has been our experience that after topectomy as after lobotomy (48) seizures tend to become less frequent with the passage of time.

Electroencephalograms (EEG): The electroencephalogram has been somewhat abnormal after topectomy in a few patients who have not suffered seizures after operation, while in one of three cases with a "borderline" abnormal EEG before operation seizures did develop.

The EEG for a few weeks after topectomy, as it may after lobotomy, cortical undercutting, (47) and sometimes electroshock therapy, generally shows abnormalities. The prefrontal, precentral and sometimes the temporal leads are the most apt to show changes after topectomy. In some cases in whom traces of these changes persist for months no seizures have developed, while in a few other patients, despite an apparently normal post-operative EEG several months after operation, one or more seizures have occurred. Thus, EEG findings are not infallibly correlated with post-operative seizures.

Six months or so after topectomy approximately two-thirds of the patients tested have had EEG records reported as being within normal limits while the remaining third have had some abnormal findings in the frontal and occasionally in the anterior temporal leads also.

Psychometric tests: The psychometric tests before and after topectomy in this series indicate that the I.Q. has seldom been appreciably altered by topectomy, unless for the better because of reduced anxiety and tension. In some cases there has been a narrowing of the field of interest, in others an increase, while in most of the improved patients there has been evidence of a greater interest in social relations associated with a reduction of anxiety. For more detailed accounts of this subject the reader is referred to the first Columbia-Greystone Project (2), early topectomy reports (1),

(17) and the more recent reports of Landis (49), Hoch (33) and Cattell (34).

Electrical studies: During the course of identifying various parts of the cerebral cortex by means of accepted techniques of electrical stimulation in this and other topectomy series (2), (4) there was no evidence that the threshold of excitability of the primary motor cortex was abnormal in any of these psychotic patients.

The rostral cingulate, anterior temporal and posterior orbital cortex and the uncus yielded respiratory changes (37), usually in the direction of brief temporary slowing or transitory apnea and an occasional brief alteration in pulse rate and blood pressure, on electrical excitation. The uncus generally responded at the lowest thresholds of square wave stimulation (37), which were comparable to the parameters yielding motor responses from the precentral gyrus (4). The anterior temporal cortex close to the sphenoid ridge and the posterior portion of the orbital cortex had higher thresholds, while the parolfactory area and the rostral cingulate had the highest. Bilateral pupillary dilatation was frequently observed coincident with stimulation of the anterior cingulate cortex. Many of the effects reported above have been obtained on stimulating the corresponding cortical regions by Livingston et al. (39) and Scoville et al. (40) in man, and by Kaada, Pribram et al. (38) in the primate. Stimulation of closely adjacent and more remote portions of the frontal and temporal cortex at the same parameters did not yield such changes. Other control measures which were also taken (37) confirm our impression that respiratory, vasomotor and pupillary responses may be obtained by electrical excitation of the regions just described and not by adjacent structures or adjacent cortex under similar circumstances. EEG changes associated with studies of this kind carried out in state hospital investigations will be reported in detail in another communication.

Improvement rating: In the following rating of results in this series of post-topectomy patients the total number of significantly improved cases from the psychiatric point of view is 45 of the 99. The few cases lacking recent follow-up data are considered to be still in the un-improved group and have been so listed. Of the 45 significantly improved patients 34 are socially rehabilitated or 34% of the 99 cases in the series (*Table IV*). The remaining 11 of the 45 cases showing significant improvement, but not social rehabilitation, were mostly assaultive schizophrenics, predominately of the paranoid type, who manifested significantly *good* palliative effects following topectomy. Five of these 11 are home, three are in mental homes at the insistence of their families and one by her own request, despite repeated urging on the part of her family and the psychiatric staff. The remaining two represent good palliative results with respect to relief of pain due to carcinomatosis. Eleven other cases have been listed in *Table III* as showing insignificant or no improvement even though a number have been discharged to their homes with a fair degree of palliative improvement, for every effort has been made by the psychiatrists who evaluated the cases in this series to be as conservative as possible in their ratings.

The best results are therefore represented by the 34% who have been socially rehabilitated, which means that in addition to their psychiatric improvement these patients have shown a consistent ability to manage their households and personal finances, do their shopping, entertain and travel independently, and/or to earn their living at their original pre-illness occupation or the equivalent. No deteriorated schizophrenic patient however has attained a rating of social rehabilitation.

Illustrative of socially rehabilitated patients are the following examples: The guardianship of person and property has been restored to one paranoid schizophrenic patient by court action two years after topectomy, so that she is now legally as well as psychiatrically regarded as being well and fully competent. She is moreover working besides leading a normal life. Another chronic though not deteriorated

schizophrenic young woman of 34, who had been plagued for 12 years with severe paranoia punctated by increasingly frequent agitated, assaultive or depressed states and auditory hallucinations, has been completely restored to society since her topectomy over two years ago. She no longer suffers hallucinations and her friends say that she seems entirely normal. Indeed, according to her old friends and the referring psychiatrist her personality has undergone an up-grading rather than a down-grading since operation. In this respect a leading neuro-psychiatrist who referred two severely depressed suicidal patients for topecomy, states that after operation neither patient has shown evidence of personality or intellectual deterioration as far as he can determine, having known both for over 20 years before their illness began. Both these ladies furthermore are now managing their households, social engagements and financial affairs. A schizophrenic male in his fifties has been running his own international business firm most successfully since topectomy, and has made several trips to foreign countries with his family for business purposes and vacations in the ensuing three years.

Of the obsessive tension states one woman who had become literally trapped in her room by progressive compulsions, has earned her own living since topectomy over two years ago, has paid off her insurance debts, and has been handsomely remunerated for a magazine article she wrote since operation. Another patient of this group has been restored to her home life and its normal activities, while still another has been engaged in an active, complicated and important accounting job since his topectomy more than two and a half years ago.

While topectomy offers no better over-all results from a statistical point of view than prefrontal lobotomy (8), (10), (10a), (14a),

TABLE IV

Asterisk (*) Draws Attention to the Fact That Other Patients, While Benefited by Topectomy so That They Have Been Able to Work, Are Not Sufficiently Improved to be Considered "Socially Rehabilitated."

PRESENT STATUS OF SOCIALLY REHABILITATED PATIENTS

34 OF 99 Cases (34%)

	MANAGING HOUSEHOLD	WORKING	
Schizophrenic: (68)			
PARANOID	9	4	
CATATONIC	1	0	
HEBEPHRENIC	0	1	
PSEUDONEUROTIC	3	3	
	13	8	= 21★
Other: (31)			
OBS.—COMP.	1	2	
MANIC—DEP.	1	0	
AG.—DEP.	2	0	
INVOL.—DEP.	2	0	
REACT.—DEP.	2	1	
ALC. AND DRUG	1	1	
	9	4	= 13
		Total—34	

(45), etc. or allied procedures such as cortical undercutting (35), individual cases that achieve maximal improvement after topectomy do not show appreciable down-grading of the personality nor significant intellectual deficit, so that the operation is elected by a number of psychiatrists (17), (33) in preference to other operative procedures, which carry a greater risk of adverse personality and intellectual effects, a higher operative mortality rate, and the possibility of lasting urinary incontinence. Indeed, with two possible exceptions, there is no evidence that topectomy rather than the psychosis has made any patient worse.

The best all around results after topectomy of the so-called area 9, subtotal "9–10" or polar "10–11" type have occurred in patients suffering from agitated or involutional depressions, obsessive-compulsion states, or the pseudoneurotic form of schizophrenia. The paranoid type of schizophrenia responds next best, while the catatonic, hebephrenic and chronic deteriorated schizophrenics as a rule tend to show little or no improvement after topectomy.

As to those patients who have had two separate operations upon the brain, of the seven who had not responded to transorbital lobotomy three have responded well to subsequent topectomy: one was a pseudoneurotic schizophrenic, one a paranoid schizophrenic, and one a manic-depressive psychosis of depressed type.

After a second operation on seven other patients, four have been significantly improved to the point of social rehabilitation while three were not improved. Five of the seven were chronic but not deteriorated schizophrenic patients, four being of the paranoid type. Two of the latter have been socially rehabilitated. A fifth case in this improved category suffered from an obsessive-compulsive neurosis and a sixth from involutional melancholia that did not respond to psychotherapy or shock therapy. None of these four improved cases, of course, had shown significant improvement after their first topectomy.

Two hebephrenic schizophrenics, on whom respectively an area 9 and a subtotal "9–10" topectomy was done two years after prefrontal lobotomy, failed to show significant improvement though both were slightly better. Of four patients submitted to prefrontal lobotomy after topectomy none improved, three being frankly schizophrenic while one suffered a severe anxiety state with underlying schizoid manifestations. Krueger (36) however describes seven unmanageable deteriorated schizophrenic patients who were only temporarily benefited by topectomy as to behavior, and were later subjected to prefrontal lobotomy after relapse. Of these seven, four have shown palliative improvement as to behavior after subsequent lobotomy. These cases, then, also serve to illustrate the importance of the quantitative factor (a second operation) in the surgical treatment of mental illness.

Discussion: While the symmetrical bilateral frontal lobe ablations described in this communication were planned and carried out as accurately as possible, absolute precision as to the site of cortical resections has of course been impossible owing to variations in cerebral size and configuration or in the degree of atrophy found at operation. Some variations in these cortical resections were also imposed by the necessity of altering their shape or dimensions according to sulcal or vascular patterns, previous operative intervention, or the condition for which the patient was operated upon, as already indicated. It should also be emphasized again that ablations according to cytoarchitectonic areas can at best be considered only a rough approximation.

Finally, while the dimensions of resected cortex have been estimated in all cases, the actual weight or volume of the specimens from some of the earlier cases was not determined. Instead, the weight or cubic volume (which are practically the same for brain tissue) was estimated from the measurements of the operative cavity. Despite all these factors, however, it is felt that a reasonable degree of accuracy as to the location of these ablations has been attained, as checked by reference to the excitable motor cortex and rostral cingulate cortex at operation in a number of cases, by post-operative x-rays of the skull in almost all cases

(the location of ablations being indicated by silver clips), and by autopsy in two cases who died over two years following topectomy. (One death was traumatic; the other followed a prefrontal lobotomy.) At this juncture it should also be emphasized that all ablations included the corresponding or adjacent cortex of the medial or parasagittal aspect of each frontal lobe along the falx, together with the cortex removed from the convex or from the ventral surfaces.

While ablations in the region believed to represent Brodmann's area 9 apparently followed the gross outline of that area reasonably closely, the extreme caudal portion or tail of area 9 was usually subtotally removed. The subtotal removals of areas 9 and 10 listed as "9–10" topectomies included resection of the rostral and medial portions of what was judged to represent these areas and spared most or all of both frontal poles. Thus the "9–10" ablations were more rostrally situated than the area 9 ablations, while the polar type of topectomy involved resection of cortex from an even more rostral and ventral location, presumably including the bulk of area 10 plus the rostral half of area 11, which together of course included the frontal poles. A fourth type of ablation, the orbital (principally area 11) was not carried out in this series but has been carefully studied in other topectomy series (2), (4). It consists of bilateral symmetrical removal of the orbital gyri to within 0.5–1.0 cm of the optic chiasm, care being taken to preserve the olfactory tracts in removal of cortex from each side of each tract. This type of ablation principally involves area 11, together with some of area 10, and is shown diagrammatically in *Figure 2* solely for purposes of comparison. By actual weight rather than volumetric estimation, over 100 cases in this and other series have now been done with an equivalent amount of cortical removal with each of the following three types of ablation: Rostro-medial (subtotal areas 9–10); Polar or prefrontal (subtotal areas 10–11); and orbital (principally area 11). In the opinion of consulting and referring psychiatrists there has been no essential difference in post-operative behavior or results following these different types of ablation.

There has been for example no greater tendency to undue restlessness, pacing or hyperactivity following orbital ablations (4) than after ablations from the other sites under consideration. Indeed, *in general* it seems that the immediate post-operative reaction and behavior after any of these different types of topectomy tends to parallel and frequently accentuate the preoperative behavior tendencies of the patient. Thus a restless excitable individual tends to show more pronounced characteristics of the same kind after any of these three types of topectomy operation while the quiet listless patient is apt to be even quieter during the immediate post-operative period. Exceptions of course have been observed.

There have been, moreover, no obvious enduring gross alterations in the function of the autonomic nervous system characteristic of one type of ablation as contrasted with another. A few patients have put on weight after each of these types of topectomy, but this can be attributed to reduction in anxiety and tension, as can the post-operative arrest of the signs and symptoms of proven ulcerative colitis in another case of this series. Nor have any trophic changes or early deaths occurred in any of the ventral ablations involving resection of posterior orbital cortex as suggested by McLardy and Meyer (12). Finally, no significant difference has been apparent as to the percentage of good clinical results after ablation from a given site as contrasted with another site, provided the amount of ablated cortex is equivalent for cases of a given category. This opinion is based on careful evaluation of the cases in this series as well as those of a larger state hospital series (4), (33). The fact that certain patients have remained greatly improved after relatively small area 9 ablations (as contrasted with larger "9–10" or "10–11" ablations) may be attributed to the fact that most of these improved area 9 cases suffered primarily from affective disorders for which removal of less tissue is more apt to be of help than it is in schizophrenia, as pointed out elsewhere.

These considerations, in the opinion of the author, indicate that the *amount* of cortex removed *rather than its location* is the important factor in frontal lobe surgery for the treatment of mental illness. This principle, also advanced by Percival Bailey (41), McLardy and Meyer (46) and Lashley (42), is stressed again because of a recent suggestion to the contrary (25).

In considering both the selection of patients for topectomy and the post-operative clinical results, it must be borne in mind, as emphasized by Donovan et al. (43), Hoch (33) and others, that frontal lobe surgery for some cases is elected only as a palliative measure to render the patient more manageable, while for others it is done with a greater expectation of achieving a high degree of improvement that may be rated as "good" or "significant" to the point of "social rehabilitation". However, the cortical ablations mentioned in this discussion of topectomy are in general not sufficient as to quantity to achieve a palliative improvement in the *deteriorated* schizophrenic patient, Krueger (36) having had a similar experience.

In contrast to this, among 21 patients of the New York State Hospital group (4) suffering from a pseudoneurotic form of schizophrenia (obsessive-compulsive and phobic manifestations plus an underlying structure of schizophrenia), who did not show any apparent deterioration, 62% showed a "good" improvement (33) following topectomy either of the "9–10", the polar, or the orbital type. Hoch also states (33) that "Markedly aggressive patients seemingly respond better to lobotomy than to topectomy", but that after topectomy, "Our clinical impression is that marked alterations in personality especially in the well-known apathy, complacency, and emotional dulling do not occur as frequently and persistently as with lobotomy."

How or why topectomy, lobotomy or allied procedures in the field of psychosurgery are effective remains a mystery, and much the same might be said of electro-shock therapy, as indicated by a recent article entitled "Fifty Theories of Shock Therapy" (50). The factor of "total push" certainly does not explain the observed post-operative improvement since most of these patients had been subjected to diligent psychotherapy and family interest, in addition to other forms of treatment such as electric and insulin shock therapy prior to operation. The total push factor furthermore seems to have been ruled out, with possibly a few exceptions, by the first Columbia-Greystone study (2). The shock effect of an intracranial operation of itself hardly serves to explain improvement, for in a second state hospital project (3) craniotomies carried out on psychotic patients without direct surgical intervention upon the frontal lobes failed to induce a significant number of improvements. Furthermore, some of the patients in the present group of 99 cases serve as their own controls in this respect, for a number of them after an initial topectomy had failed, later improved after a second topectomy or a subsequent lobotomy.

Most authors on the subject of frontal lobe surgery advance the theory that mental illness is relieved by interruption of connections between the dorso-medial nucleus of the thalamus and the frontal cortex (8), (45), (46). It has also been postulated that secondary and/or direct alterations of hypothalamic function may follow operation and may contribute to the post-operative improvement of the psychotic patient because of changes not only in thalamic but also in hypothalamic function capable of influencing the emotional background of the patient. More widespread post-operative changes in other parts of the brain may also play an important therapeutic role, perhaps by alterations of cortico-cortical as well as subcortical cortical neural circuits. This premise is suggested by the fact that post-mortem lobotomy studies have shown changes in the cerebral cortex and white matter in some cases well beyond the confines of the lobotomy incisions and also subcortical degeneration in structures other than the thalamic nuclei (11), (46). Furthermore, when post-lobotomy pneumoencephalograms have been compared with pre-lobotomy gas studies evidence of widespread post-operative cortical and subcortical atrophy has been present in some cases (43), (51).

Perhaps therefore, as Yakovlev, Hamlin and Sweet have said (11), degeneration of anterior thalamic radiations and thalamic nuclei following frontal lobotomy have been stressed to the "exclusion of the even more obvious degeneration of the far greater mass of efferent projections which connect the frontal lobes to all levels of the neuraxis. . . ." Extensive changes of this sort may partly explain why special psychometric tests devised by Landis, Zubin and Mettler (49) and others suggest to them that perhaps "psychosurgery of the frontal lobes results in a narrowing of the field of attention so that there is a tendency for the patient to be stimulus-bound", or that perhaps "The surgery adds to the mental confusion of the patient. This confusion grows out of an interference with the associative bonds linking the mental elements. . . ." It is hard for the writer to see how improvement and social rehabilitation can occur if surgery *adds* to the mental confusion of the patient. However operation must interfere with associative bonds in a psychotic individual and thus help to alter abnormal neural patterns serving to perpetuate psychotic behavior.

Since the actual site of frontal lobe surgery does not seem to be of paramount importance in psychosurgery, but rather the quantitative factor of the surgical intervention, it would appear that the extent to which abnormal associative patterns are interfered with by surgery upon the brain may be one of the major elements in psychosurgery. This concept is important for two reasons: first of all, it emphasizes the need to select carefully the type of operation according to the requirements of each case instead of using the same sort of operation for every psychotic patient for whom brain surgery is recommended. Secondly, this concept tends to abolish the idea of specificity of function of the prefrontal cortex, for which there seems at present to be no good evidence, and supplant it with the principle so well epitomized by Lashley (42) to the effect that "The trace of any activity . . . is tied in with the whole complex of spatial and temporal axes of nervous activity which forms a constant substratum of behavior."

SUMMARY

1. The advantages of bifrontal topectomy are: (a) An operative mortality rate of zero; (b) An operative exposure sufficient to permit the surgeon not only to gauge the site and extent of the operative procedure with reasonable accuracy, but also to make observations regarding the electrical activity and the threshold of electrical excitability of various parts of the cortex, designed to be of ultimate potential help to each individual case as well as perhaps to all cases of advanced mental illness for whom brain surgery may be indicated; (c) It is felt that topectomy carries less risk of personality and intellectual impairment, and of loss of sphincter control, than standard prefrontal lobotomy, so that topectomy is therefore particularly recommended for non-deteriorated cases of mental illness for whom brain surgery is advised.

2. The disadvantages of topectomy are: (a) Failure to effect palliative improvement in chronic deteriorated schizophrenic patients because it is not a sufficiently radical operative procedure as to the quantitative factor; (b) A somewhat higher incidence of post-operative seizures (16%) as compared with an average of approximately 12% or higher after prefrontal lobotomy; (c) The fact that topectomy is a more elaborate, painstaking and therefore more time-consuming surgical procedure than lobotomy.

3. A survey of these 99 cases shows that while 15 had one or more post-operative seizures, 4 of these had a second operation (which is a factor that raises the seizure incidence) (8); another 4 had no more than two seizures apiece, and 4 others had evidence of some predisposing convulsive factor, leaving only 3 who developed more than two post-operative seizures without a predisposing factor other than the operation itself. In most of these cases moreover the frequency of seizures has decreased with the passage of time, as after lobotomy (48), and no case with one possible exception has been prevented from being restored to society or been unable to work solely because of seizures. No patient save one developed seizures pro-

vided he has been seizure-free for one year following topectomy. When seizures have occurred, they usually happened between the fourth and thirteenth post-operative months.

While the actual technique of surgical ablation seems to have little bearing on the incidence of seizures, it is tentatively suggested that the *site* of cortical ablation bears a relation to the post-operative seizure incidence, for the incidence has been lower in this and other topectomy series following the more rostral and more ventrally placed ablations of frontal cortex, perhaps because they are further removed from the motor cortex, or perhaps because they require less extensive ligation of the superior cerebral veins.

4. There seems to be no significant relation between the site or location of frontal lobe ablations and the percentage of cases showing post-operative clinical improvement.

5. There does, however, appear to be a definite correlation between the quantity of cortex removed for various types and severities of mental illness, and clinical improvement. This premise with regard to the gray matter agrees with that expressed by McLardy and Meyer (46) with respect to the white matter, to the effect that: "There is strong evidence that, in at least predominantly affective conditions and mixed, mainly paranoid psychoses, improvement varies, among cases of equally moderate prognostic potentiality, directly with the amount of prefrontal cortex isolated from its white matter—No evidence is found of any segment of white matter the bilateral involvement of which is indispensable to improvement."

6. For other reasons given in the text, however, the site currently preferred for topectomy is the extreme rostral or polar region of frontal cortex believed to represent the rostro-ventral portion of Brodmann's area 10 and the rostral portion of area 11.

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Transactions of the Sections

SECTION ON GENERAL MEDICINE

24 January 1951[1]

Current Trends in the Treatment of Hypertension
Panel Discussion: Julian Love, Capt. (MC), USN, Moderator

INDICATIONS FOR MEDICAL VERSUS SURGICAL TREATMENT. Charles C. Wolferth, M.D.

EVALUATION OF NEW THERAPEUTIC AGENTS. Joseph H. Hafkenschiel, M.D.

TYPES OF SURGICAL TREATMENT. Harold A. Zintel, M.D.

MANAGEMENT OF THE COMPLICATIONS OF HYPERTENSIVE CARDIOVASCULAR DISEASE. Richard A. Kern, M.D.

26 February 1951

THE EFFECT OF ACTH AND CORTISONE ON THE CAPACITY TO PRODUCE ANTIBODY IN PATIENTS WITH CHRONIC HEPATIC DISEASE. W. Paul Havens, Jr., M.D., and James M. Shaffer[2], M.D. (Discusser: C. J. D. Zarafonetis[2], M.D.) (*Abstract 1, below.*)

PITFALLS IN THE DIAGNOSIS OF ADRENAL TUMORS IN PATIENTS WITH HYPERTENSION. Carl K. Friedland[2], M.D., and M. August Lindauer, M.D. (Discusser: Herman W. Ostrum[2], M.D.) (*Abstract 2, below.*)

CLINICAL AND EXPERIMENTAL OBSERVATIONS ON THE USE OF PRONESTYL IN THE TREATMENT OF CARDIAC ARRHYTHMIAS. Keehn Berry[2], Jr., M.D., E. Lee Garlett[2], M.D., Samuel Bellet, M.D., and W. I. Gefter,[2] M.D. (Discusser: Thomas M. Durant, M.D.) (*Abstract 3, below.*)

MESENCEPHALOTOMY IN INTRACTABLE PAIN. H. T. Wycis[2], M.D., and E. A. Spiegel, M.D. (Discusser: A. M. Ornsteen, M.D.) (*Abstract 4, below.*)

[1] Joint meeting with the Philadelphia Heart Association, the Postgraduate Course in Cardiovascular Diseases of the American College of Physicians, and the Staff of the U. S. Naval Hospital, Philadelphia.

[2] By invitation.

26 March 1951

GENERALIZED HISTOPLASMOSIS OF MODERATE SEVERITY IN ADULTS. Meyer Solis-Cohen, M.D., and Rose R. Ichelson[2], A.B. (Discusser: Harold L. Israel, M.D.) (*Abstract 5, below.*)

THE ELECTROKYMOGRAM IN CORONARY ARTERY DISEASE. A. Henry Clagett, Jr.[2] M.D. (Discusser: Herbert M. Stauffer[2], M.D.) (*Abstract 6, below.*)

THE TREATMENT OF THYROTOXICOSIS WITH 1-METHYL-2-MERCAPTOIMIDAZOLE. Edward Rose, M.D., R. L. Kendrick[2], M.D., and Kent F. Balls[2], M.D. (Discusser: Robert Robbins[2], M.D.) (*Abstract 7, below.*)

THE PRODUCTION AND TRANSFER OF MYELOGENOUS LEUKEMIA IN THE RAT. Harry Shay, M.D., Margot Gruenstein[2], Charles Harris[2], M.D., and Lilly Glazer[2]. (Discusser: Thomas Fitz-Hugh, Jr., M.D.) (*Abstract 8, below.*)

23 April 1951

CLINICAL OBSERVATIONS CONCERNING THE ROLE OF THE ADRENAL GLAND IN THE MAINTENANCE OF BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION. Charles C. Wolferth, M.D., Joseph H. Hafkenschiel, M.D., Harold A. Zintel, M.D., Francis D. W. Lukens, M.D., and William A. Jeffers, M.D. (Discusser: Louis A. Soloff, M.D.) (*Abstract 9, below.*)

SURVEY OF TYPHUS ANTIBODY LEVELS IN BLOODS OF INDIVIDUALS BORN IN EASTERN AND CENTRAL EUROPE AND THE UNITED STATES. Joseph C. Doane, M.D., Nathan Blumberg[2], M.D., M. Michael Sigel[2], PH.D., and Laurence B. Weiss[2], M.D. (Discusser: Charles L. Brown, M.D.) (*Abstract 10, below.*)

THE DIFFERENTIAL DIAGNOSIS BETWEEN PITUITARY AND THYROID MYXEDEMA. William H. Perloff, M.D., and Lester M. Levy[2], M.D. (Discusser: F. Curtis Dohan, M.D.) (*Abstract 11, below.*)

SECTION ON MEDICAL HISTORY

1 February 1951

THE CURSE OF ERNULPHUS. Robert J. Hunter, M.D. (Discusser: Truman G. Schnabel, M.D.)

THE CHAMBERLEN FAMILY. Mario A. Castallo, M.D. (Discusser: Bernard Bernstein[2], M.D.)

DUHRING AND DERMATOLOGY IN PHILADELPHIA. Reuben Friedman, M.D. (Discusser: Robert L. Gilman, M.D.)

15 March 1951

CHINESE HERBAL MEDICINE GIVES WAY TO MODERN MEDICAL SCIENCE. William W. Cadbury, M.D. (Discussers: J. C. McCracken[2], M.D., and Harold H. Morris, M.D.)

PLATO AND PSYCHOSOMATIC MEDICINE. Nicholas Padis, M.D. (Discusser: Earl D. Bond, M.D.)

RECOGNITION THROUGH THE CENTURIES OF THE RELATIONSHIP BETWEEN LOCAL AND GENERAL DISEASES. Meyer Solis-Cohen, M.D. (Discusser: Robert J. Hunter, M.D.)

19 April 1951

Meeting in Commemoration of Francis R. Packard, M.D., and the 200th Anniversary of the Pennsylvania Hospital

THE PERSONAL SIDE OF DR. PACKARD. Frederick Fraley, M.D. (Discusser: Charles F. Mitchell, M.D.)

THE PROFESSIONAL SIDE OF DR. PACKARD. George M. Coates, M.D. (Discusser: Robert J. Hunter, M.D.)

DR. PACKARD'S INFLUENCE ON THE STUDY OF MEDICAL HISTORY AND THE HISTORY OF THE PENNSYLVANIA HOSPITAL. Edward B. Krumbhaar, M.D. (Discusser: W. B. McDaniel, 2d[2], PH.D.)

SECTION ON OPHTHALMOLOGY[3]

18 January 1951

BIOMICROSCOPY OF THE ZONULE. Milton L. Berliner[2], M.D.

[3] The presentations at this Section are customarily abstracted in the *American Journal of Ophthalmology* and in the *A. M. A. Archives of Ophthalmology.*

15 February 1951

TRANSPLANT OF LACRIMAL SAC—STALLARD TECHNIQUE. (Moving Picture). Edmund B. Spaeth, M.D.

STUDIES OF CAPILLARY PHENOMENA IN PRIMARY GLAUCOMA. Irving H. Leopold, M.D., Arthur H. Keeney[2], M.D., and Virginia T. Keeney[2], B.S.

THE PROBLEM OF EYE CARE IN THE EVENT OF DISASTER. Victor A. Byrnes[2], Col. (MC), USAF.

15 March 1951

WOUND CLOSURE WITH CATGUT. Francis Bruce Fralick[2], M.D.

19 April 1951

BILATERAL 6th NERVE PARALYSIS: CASE REPORT. Harold Rosegay[2], M.D. (Discusser: Robert A. Groff, M.D.)

ASPIRATION BIOPSY OF MALIGNANT MELANOMA OF THE CHOROID, WITH CASE REPORT. M. Luther Kauffman, M.D.

DIBENAMINE: A CLINICAL AND EXPERIMENTAL STUDY. Samuel L. DeLong[2], M.D., and Harold Scheie, M.D.

SECTION ON OTOLARYNGOLOGY[4]

17 January 1951

THE GENETIC INTERPRETATION OF CONGENITAL ATRESIAS OF THE NOSE. J. Parsons Schaeffer, M.D.

THE SURGICAL TREATMENT OF CHOANAL ATRESIAS. Karl M. Houser, M.D. (Discusser: Oscar V. Batson, M.D.)

21 February 1951

INTRANASAL SURGERY—A NEGLECTED ART. George L. Whelan, M.D. (Discusser: B. H. Shuster, M.D.)

[4] The presentations at this Section are customarily abstracted in the *A. M. A. Archives of Otolaryngology.*

Lipoma of the Larynx. Frederick Harbert[2], Capt. (MC), USN. (Discusser: Louis H. Clerf, M.D.)

Presentation of New Instrument. Otto C. Hirst, M.D.

18 April 1951

Histoplasmosis of the Larynx. F. J. McNellis[2], M.D., and F. J. Putney, M.D. (Discusser: Robert M. Lukens, M.D.)

Spontaneous Intramaxillary Hemorrhage. Charles H. LaClair, Jr., M.D. (Discusser: Austin T. Smith, M.D.)

Presentation of "Notes on Dr. E. B. Gleason's Course in Otolaryngology at the Medico-Chirurgical College in 1901, by Dr. L. Loutfian of Turkey". Robert J. Hunter, M.D.

Showing of Codronchius' *De vitiis vocis*, Frankfurt, 1597, purchased by the Section for the College library. Robert J. Hunter, M.D.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

19 January 1951

Newer Developments in Venereal Disease Control in the United States and Abroad[5]. Norman R. Ingraham, Jr., M.D.

The Philadelphia Public Health Survey —Present and Future Aims. Clyde Arbegast[2].

30 April 1951

New Approaches to the Epidemiology of Influenza. Dorland J. Davis[2], M.D.

Influenza in Philadelphia. Angelo M. Perri[2], M.D.

Prophylaxis in Influenza. L. P. Kravis[2], M.D.

Laboratory Techniques of Influenza. M. Michael Sigel[2], PH.D.

Abstracts

Abstract 1

The Effect of ACTH and Cortisone on the Capacity to Produce Antibody in Patients with Chronic Hepatic Disease. W. Paul Havens, Jr., M.D., and James M. Shaffer, M.D.

Measurement of the capacity of Schick-negative patients with various diseases to produce diphtheria antitoxin following a single intramuscular injection of 50 Lf purified diphtheria toxoid revealed an unusual capacity of patients with chronic hepatic disease to produce this antibody as compared with control subjects. This superior performance was apparently unrelated to age, general condition of patient, the state of nutrition, amount of serum albumin and globulin, or resistance to intercurrent infection.

ACTH or cortisone was given late in the course of antibody production when the titer was declining; at the mid-point when antibody was approximately at its peak; and from the very first day of hyperimmunization. Of particular interest were the facts that (1) when these substances were administered to patients from the first day of hyperimmunization, all patients tested were able to produce diphtheria antitoxin and frequently in large amounts; (2) regardless of when these materials were given, there was no apparent qualitative alteration in the pattern of production of antibody. It is difficult to determine quantitative differences in amount of antibody with small groups of patients; however, preliminary results suggest that, although there was no qualitative alteration in the curve of production, there did occur a more rapid diminution in amount of circulating antibody when ACTH or cortisone was given.

Abstract 2

Pitfalls in the Diagnosis of Adrenal Tumors in Patients with Hypertension. Carl K. Friedland, M.D., and M. August Lindauer, M.D.

Pheochromocytomas are relatively rare tumors. Although they are most easily recognized when they give rise to paroxysmal hypertension, the majority of such tumors are associated with

[5] Printed in this issue of the *Transactions & Studies*.

sustained hypertension and therefore the diagnosis must be considered in all hypertensive patients. Several diagnostic aids are employed to supplement the clinical data. The histamine, mecholyl and etamon provocative tests may be dangerous in patients with sustained hypertension and they may give false-positive and false-negative reactions. The adrenolytic benzodioxane and dibenamine tests are useful but a negative response may occur in the presence of tumor; moreover, they may give rise to alarming reactions. The adrenalin tolerance test is subject to wide individual variations. A new adrenolytic agent, regitine, remains to be evaluated.

Radiographic data are similarly not infallible. Two hypertensive patients in whom there was roentgen evidence suggestive of adrenal tumor, were subjected to exploration but no tumor was found in either patient.

Abstract 3

Clinical and Experimental Observations on the Use of Pronestyl in the Treatment of Cardiac Arrhythmias. Keehn Berry, Jr., M.D., E. Lee Garlett, M.D., Samuel Bellet, M.D., and W. I. Gefter, M.D.

Procaine Amide (Pronestyl), a new procaine derivative which has been found useful in the treatment of rapid ectopic cardiac rhythms, was used to treat 98 episodes of arrhythmia in 78 patients. The drug was found to be effective when administered by either the oral or the intravenous route. Eleven of 17 episodes of ventricular tachycardia were converted to normal sinus rhythm, and 10 of 10 episodes of nodal tachycardia were successfully treated. In 30 out of 35 patients with multiple premature ventricular contractions, the arrhythmia was abolished by Pronestyl. The drug was, however, notably unsuccessful in the conversion of auricular flutter or fibrillation as only 1 in 21 episodes in this group was converted to a normal sinus rhythm.

Toxic signs were noted in 15 of the 98 episodes. The most serious toxic manifestation resulting from intravenous administration was hypotension, and following oral medication, nausea, vomiting, psychosis, and urticaria were noted. It is felt that the oral route is the method of choice in treatment, and doses varying from 250 mg. to 1 Gram every four hours were used effectively. One gram given at a rate of not more than 200 mg. per minute is the maximum safe intravenous dose.

Pronestyl is a valuable addition to the known methods for the treatment of rapid ectopic cardiac rhythms, particularly ventricular tachycardia.

Abstract 4

Mesencephalotomy in Intractable Pain. H. T. Wycis, M.D., and E. A. Spiegel, M.D.

By means of the stereotaxic method developed by us, lesions were placed in the pain conducting tracts at the mesencephalic level (mesencephalotomy) alone or in combination with lesions of the dorsomedial nucleus of the thalamus (mesencephalo-thalamotomy). The latter lesion was added in cases with marked emotional reaction to pain. Since patients become unconcerned about their pain following prefrontal lobotomy (Freeman and Watts), and since the dorsomedial nucleus of the thalamus degenerates following this procedure, lesions of this nucleus are added to that of the long ascending pain conducting pathways in order to induce a relative indifference to pain perceived through remaining auxiliary pathways. In two cases of thalamic pain lesions were produced in the nucleus ventralis postero-lateralis of the thalamus.

Our material consisted of 22 cases: 9 cases of pain due to inoperable malignancy; 4 cases of pain following spinal trauma; 2 cases of facial pain persisting after retrogasserian root section; 5 cases of thalamic pain; 1 case of pain following herpes zoster; 1 case of causalgia secondary to amputation neuroma. There were two deaths in the tumor group. Both patients were in an advanced cachectic state. There was no fatality in the non-tumor cases.

Abstract 5

GENERALIZED HISTOPLASMOSIS OF MODERATE SEVERITY IN ADULTS. Myer Solis-Cohen, M.D., and Rose R. Ichelson, A.B.

Nearly all the reported cases of generalized histoplasmosis have been severe, most of them fatal, the majority diagnosed post mortem. A few patients, mostly children, with active clinical manifestations have survived.

Two generalized cases of moderate severity in adults are herewith reported in which *Histoplasma capsulatum*, pathogenic for the patient, have been recovered from cultures in a new fungus culture media from the nose, throat, nasopharynx, gums, rectum and feces, which caused death in inoculated animals with recovery of *Histoplasma* from their organs.

Such cases and cases caused by other fungi are believed to be more common than suspected. A diagnosis of "yeast cells" should never be accepted. Such cells should be identified and tested for pathogenicity for laboratory animals and for their host. They should always be reported, even if considered contaminants. When fungi are discovered, cultures should be made to determine whether the infection is generalized. In difficult and undiagnosed cases cultures should be made for bacteria and fungi. It is unscientific to assume a fungus is nonpathogenic without tests for pathogenicity. Studies should be made on the transmissibility of fungus diseases. Should not public health laboratories be equipped to conduct mycological investigations, without cost to the poor?

Abstract 6

THE ELECTROKYMOGRAM IN CORONARY ARTERY DISEASE. A. Henry Clagett, Jr., M.D.

Electrokymograms have been obtained in approximately 200 patients with coronary artery disease.

1. The electrokymographic examination must be complete, as it is not unusual to find abnormalities occurring in only one small segment of the ventricular contour.

2. While a normal electrokymogram suggests a normal heart, one patient developed acute myocardial infarction eight weeks following a normal examination.

3. On the other hand, while an abnormal electrokymogram suggests the presence of heart disease, paradoxical pulsations do not necessarily indicate myocardial infarction. Furthermore, an area of infarction cannot be localized by the electrokymogram.

4. An equivocal finding is delayed systolic ejection, or lateral border motion, confined to early systole. This finding was the sole abnormality in many patients showing other evidence of severe myocardial damage. It is found, however, fairly frequently in patients with no evidence of cardiac disease and is thought to be due to positional changes. This phase of the subject is undergoing extensive clinical evaluation.

At the present time, while the electrokymogram is primarily a research tool, it appears as though it may be helpful in supplying an additional objective test in the case of the patient with borderline findings. In fourteen patients whose histories were typical of organic heart disease, an abnormal electrokymogram was the only objective evidence of pathology.

Abstract 7

THE TREATMENT OF THYROTOXICOSIS WITH 1-METHYL-2-MERCAPTOIMIDAZOLE. Edward Rose, M.D., R. L. Kendrick, M.D., and Kent F. Balls, M.D.

The results of treatment with 1-methyl-2-mercaptoimidazole (Lilly) over periods of time up to 11 months in 32 selected thyrotoxic patients are reported. Seventeen were of prolonged therapy; fifteen were preoperative.

Twenty-six patients showed a good response; five, a fair response, and one, a poor response.

Untoward reactions were limited to three patients and consisted of maculopapular and vesicular skin eruptions, urticaria and pruritis. Factors other than methylmercaptoimidazole may have been responsible for these reactions.

Abstract 8

THE PRODUCTION AND TRANSFER OF MYELOGENOUS LEUKEMIA IN THE RAT. Harry Shay,

M.D., Margot Gruenstein, Charles Harris, M.D., and Lilly Glazer.

In the course of experiments with Wistar rats in which methylcholanthrene was instilled into the stomach, nine cases of leukemia (six lymphatic and 3 myelogenous) developed. Successful and uniform transfer of the lymphatic leukemia has been reported previously.

The myelogenous leukemia has also been transferred successfully in a very high percentage of cases to very young rats of our own Wistar colony as well as to Long Evans and Sherman strain animals. All animals used were random bred.

All transfers developed as chloroleukemias, although we had not noticed any green color in the tissues of the animals in which the disease was induced by the carcinogen. Transfer has best been obtained by the intraperitoneal injection of 0.2 cc. of positive blood and diagnosis is always made first from peripheral blood smear and confirmed later by bone marrow and tissue examination. Transfer can also be made subcutaneously. By this route local chloromata at site of injection as well as the leukemia develop.

The unquestionable nature of the leukemia, its high degree of transferability, and the uniformity of the pathologic picture obtained on transfer should make it a very useful tool in the experimental investigation of myelogenous leukemia.

Abstract 9

CLINICAL OBSERVATIONS CONCERNING THE ROLE OF THE ADRENAL GLAND IN THE MAINTENANCE OF BLOOD PRESSURE IN PATIENTS IN HYPERTENSION. Charles C. Wolferth, M.D., Joseph H. Hafkenschiel, M.D., Harold A. Zintel, M.D., Francis D. W. Lukens, M.D. and Wm. A. Jeffers, M.D.

Sixteen patients were subjected to unilateral adrenalectomy in connection with the second stage of the Smithwick type thoraco-lumbar sympathectomy. The results did not appear to be superior to those anticipated from the thoraco-lumbar operation alone. The next step included more radical excision of adrenal tissue ranging in 23 cases from the removal of approximately 90% to complete adrenalectomy. This procedure was used only in cases of advanced disease regarded as unpromising candidates for thoraco-lumbar sympathectomy. Four deaths have occurred, 2 about one week after operation and 2 later from recurrent cerebral vascular episodes.

The arterial blood pressure has been reduced in some but not in all cases from extremely high levels to a normal range by subtotal adrenalectomy alone with marked symptomatic improvement, relief from heart failure, improvement in renal plasma flow and reduction in cerebral vascular resistance.

The combination of subtotal adrenalectomy and limited sympathectomy has yielded more consistently good results than adrenalectomy alone, although many more cases and longer periods of observation will be required to warrant a conclusion. In one patient among the original group of 16 subjected to bilateral thoraco-lumbar sympathectomy and unilateral adrenalectomy, in whom that operation had failed to control severe hypertension, the blood pressure has been maintained in a low normal range for over a year following the removal of approximately 90% of the remaining adrenal gland.

If the combination of subtotal adrenalectomy and sympathectomy proves to be the most effective surgical attack on hypertension, its most effective control by non-surgical methods may require the combination of depression of adrenal cortical function and sympathetic nervous system activity.

Abstract 10

SURVEY OF TYPHUS ANTIBODY LEVELS IN BLOODS OF INDIVIDUALS BORN IN EASTERN AND CENTRAL EUROPE AND THE UNITED STATES. Joseph C. Doane, M.D., Nathan Blumberg, M.D., M. Michael Sigel, PH.D., and Laurence B. Weiss, M.D.

It was felt that a mass serologic survey of a number of consecutive hospital ward admissions might answer the question of presence of typhus antibodies in the two groups. Places of

birth were not known to the laboratory until the tests were completed. A control group, consisting of inmates of a penal institution and of a small number of doctors on the staff of Jewish Hospital, was included in the survey. Serum samples were tested in the complement fixation test by the method previously described, with the following results:

1. In a group of 69 individuals born in Eastern Europe, 12 (17%) possessed antibodies to epidemic typhus rickettsia. In a group of 80 individuals of a similar economic background but who were born in this country none possessed these antibodies.

2. In a small control group of physicians only one possessed these antibodies. The significance of this finding is doubtful because this individual, though born in Europe, was also recently vaccinated against typhus.

3. In a group of 92 inmates of a penitentiary only 2 showed these antibodies. It is possible that these resulted from vaccination against typhus.

The definite correlation between the presence of anti-typhus antibodies and residence in Eastern and Central Europe implies that these antibodies represent previous infection with epidemic typhus. The long persistence of these antibodies after the individuals had left an area where typhus is prevalent is consistent with the survival of rickettsia in latent form for long periods.

The washed rickettsial antigen was again found to be more specific than the soluble antigen. Nevertheless, the soluble antigens were found to be of great value in the diagnosis of Brill's disease and also for the purpose of this survey.

Abstract 11

THE DIFFERENTIAL DIAGNOSIS BETWEEN PITUITARY AND THYROID MYXEDEMA. William H. Perloff, M.D. and Lester M. Levy, M.D.

Patients with pituitary myxedema seem to have a higher level of thyroid function than do individuals with thyroid myxedema, as evidenced by the higher I 131 uptakes, the higher BMR's, and the lower serum cholesterols.

The use of thyrotropic hormone (T.S.H.) in conjunction with a radioiodine tracer test has proven to be an accurate method of distinguishing known cases of pituitary from thyroid myxedema. The 24 hour uptake of radioiodine was measured. Two to four weeks later, three consecutive daily intramuscular injections of 20-30 mgms. of thyrotropic hormone (Armour) were administered, and the test repeated on the following day.

Euthyroid individuals showed a mean increase of 20.8%. Primary hypothyroid patients maintained a radioiodine accumulation (7.6%) similar to their low control values (6.1%). Pituitary hypothyroid patients showed a mean increase of 32.2%; their mean post-stimulation value of 45.4% being almost identical with that of the euthyroid group (44.4%).

The results of the T.S.H. test appear to be reproducible in the same patient, and do not seem to be affected by small doses (one grain/day) of desiccated thyroid.

Proceedings of the Section on Medical History Devoted to the Late Francis R. Packard and the 200th Anniversary of the Pennsylvania Hospital*

PROGRAM

The Personal Side of Dr. Packard. Frederick Fraley, M.D.
Remarks by Charles F. Mitchell, M.D.†

The Professional Side of Dr. Packard. George M. Coates, M.D.
Remarks by Robert J. Hunter, M.D.

Dr. Packard As a Student of Medical History and Especially That of the Pennsylvania Hospital. Edward B. Krumbhaar, M.D.
Remarks by W. B. McDaniel, 2d, Ph.D.

The Personal Side of Dr. Packard. Frederick Fraley, M.D.

I feel very grateful for being allowed to share in this tribute to Dr. Packard, who was a man of unusually varied talents. As a friend of long standing, I will perhaps be able to give you a little idea of the personal characteristics that endeared him to those who were admitted to his friendship.

An ever warmer friendship of more than fifty years contains so many memories that time would not suffice to linger over them, as one may do over a loved book of verse.

It was as a student that I first came under the spell of Frank Packard's charm, while I was still an undergraduate in the Biological course at the University of Pennsylvania.

Visiting the old Pennsylvania Hospital on Pine Street not far from Independence Hall, there was among the internes there a young doctor already engrossed in the treasures of the library (though not to the detriment of his duties), broadening and sharpening a mind, and a wit that were later to enlighten and entertain those who were fortunate enough to be in his company.

This young student was immediately attracted by his beaming countenance and engaging conversation, and there the seed of appreciation was planted that grew steadily thereafter into a sturdy flowering perennial.

At the delightfully informal University Club which then occupied a small house on Walnut Street below Juniper, I occasionally was welcomed by him, and a number of his closer friends, and there, in an atmosphere of increasing intimacy became more and more aware of the magnetism that was characteristic of his nature. This magnetism increased as he went through life, attracting people of widely different interests into the field of his friendship, as the needle of the compass seeks the pole. He was a delightful "raconteur" and many of us will remember his chuckling "Did I ever tell you about the time," as he started one of his anecdotes. He was also an attentive listener but he suffered "bores" not too gladly, and one might be aware of his fading interest by a certain resigned placidity of expression such as Buddhist devotees employ in their contemplations.

It is not for me to dwell upon his professional attainments and the honors, so richly deserved, that followed his distinguished career in Medicine. Others can and will do so far bet-

* The meeting was held at the College, 19 April 1951.

† Dr. Mitchell's remarks, not written down, were unfortunately not made available for publication.

ter than this confrère. There is, however, a brief chapter in his early medical teaching that may be overlooked by his biographer, and in that chapter I played a minor rôle.

One of the subjects taught in the third year of the medical curriculum was Therapeutics, dealing with drugs, their effects, indications for their use, symptoms of overdosage, poisons and their antidotes. Our professor was the great Horatio C. Wood, vastly popular with the students, and a magnificent figure of a man who could instruct and entertain at the same time. He looked like the majestic Prospero in "The Tempest," lordly, wise and benign, but he also had an Ariel, who accompanied him into the lecture room and clinic, and that blithe spirit was Frank Packard.

Frank, in order to supplement his, at that time, not too great income, prepared a course of notes on the lectures, and "quizzed," that is to say supplemented them by holding sessions, where the students who purchased and studied his notes, had the benefit of his questions and then the correct answers, if they were stumped, as was not infrequently the case.

I still possess a well-worn copy of those notes (annotated in a somewhat Rabelaisian manner by myself), which enabled me among others to pass the stiff examination in that subject. The earnestness of his teaching is attested by the fact that as the final day approached he asked us to the house that he shared with three other bachelors (and lifelong friends), in order to more fully quiz us to the "sticking point," so that we'd not fail. This I remember with gratitude, and also the beer he provided and excellent tobacco, which added zest to the process of what might have been dryer learning. One of our classmates, who later became the distinguished Surgeon General of the United States Army,[1] carried off the annual prize offered for the best examination in that subject. The rest of us, including later lifelong friends of his such as Arthur Newlin, George Norris and Ned Hodge, passed, more or less creditably, according to our attention to, and retention of his thorough preparation.

[1] Major General Charles R. Reynolds.

In the course of time I became a "Resident," as the internes were then called, of the same historic Pennsylvania Hospital, and there had the privilege of seeing his work as one of the younger "Chiefs" in the speciality in which he was already making a reputation for diagnostic acumen and operative skill. His friendliness to all was as natural to him as breathing, and he had an "Aura" of good will spiced with humor, that was a potent stimulant to his associates, who hailed the privilege of accompanying him on his rounds.

I will only touch briefly on his literary contributions to the history of Medicine. His books were fascinating and I remember how my parents read them with as much pleasure as I did. One of my precious possessions is a copy of "The Gold-headed Cane"[2] inscribed to me by him.

He wrote the preface to the small volume that describes the Cane's progress from the hands of one celebrated physician to another, till at last it was deposited in the Museum of the College of Physicians in London. That Cane would have gained further distinction had fortune ordained that Frank Packard in his day might have become its honored custodian.

It was when I became a member of the Shakespere Society of Philadelphia that I discovered what an outstanding Shakesperian scholar Frank was. Not only was he thoroughly familiar with the plays we read, but he was at his best in the discussions not only of the medical points that arose, but also the contemporary history and literary allusions that proved his all around knowledge of the related periods both in England and in France that were a revelation to his listeners around the table. Regarding the profound interest he took in Shakespeare's plays, he naturally became especially absorbed in their medical aspects and found time to make voluminous notes, with the intention of publishing a pamphlet on "The physicians of Shakespeare's plays." However, he was never able to complete this project, but those notes I have had the opportunity

[2] By William Macmichael, M.D.

of reading. A brief paragraph from one of them is typical of his investigation, and the conclusions he reached. Writing of "The mind, the soul and the animal economy," he says, "It has interested me very much, however, to find that with all due allowance for poetic license, Shakespeare's utterances on anatomical and physiological matters were always in close accord with the opinion of the learned of his time and that his psychological surmises, were based on the best scientific knowledge of human structure and function *then* current." "Speculation ran high, especially as to the seat of the soul, and of the various animal passions, such as love, hate, valor, fear, etc." "Many attempts were made to correlate not only the physical constitution of the microcosm, Man; but also his mental and emotional nature as affecting his relations with the Macrocosm, or World." Frank was, also, par excellence, an authority on Montaigne whom he so greatly admired, and he was well versed in Voltaire, whom at times he resembled, *and* whose devastating sarcasm he was well equipped to employ, but chose instead the subtler method of a keen and ready wit, with less acerbity.

It was in 1927 that my wife and I had the great privilege of being in Rome, and again in Paris, at the same time Frank and Rita Packard were there. You can imagine what that meant to us to join their company and to learn so much about Ancient Rome, Mediaeval France, Renaissance Florence, and later periods of great historical interest from such a master of lore and learning.

In Paris Frank was a marvellous guide, knowing all the rarely visited places of interest, as well as the best cafés and superlative restaurants. He was as thoroughly familiar with Paris and its environs as the guide, who took us later on a tour of the battlefields and the city of Verdun, knew the country around it. An amusing incident on that strenuous day of tour was our partaking freely of champagne from paper cups at Épernay, while on the train at nine o'clock in the morning, having left Paris shortly after six.

Our mutually close friends Mr. and Mrs. Brinley were also on that tour, and I shall never forget the dinner that we six enjoyed at Rheims, on the last lap of that wonderful but exhausting day. I wish that we might have aptly said, as a fitting climax to the banquet, "Oh to be in England when Frank Packard's there." I can only imagine what would have been the delights of London in his happy company.

He was the most agreeable companion, either alone or enriching the society of others, that can be imagined. As was once said of another great physician, "He lived more in the sunshine of life than any man I knew." "His cheerfulness, and equanimity of temper, and kindness of heart, endeared him to a large circle of devoted friends, of whom only a few survive to commemorate his engaging qualities, and to deeply regret his loss."

The Professional Side of Dr. Packard.
George M. Coates, M.D.

Dr. Packard entered his professional life with a family medical tradition already established. His father, Dr. John H. Packard, was surgeon to the Pennsylvania and Episcopal Hospitals, his colleagues being Dr. John Ashhurst, Professor of Surgery in the University of Pennsylvania, Dr. Thomas G. Morton, and Dr. Richard Harte. His brother, Dr. Frederick A. Packard, was a young and brilliant junior physician in the Out-Patient Department, whose career was ended prematurely in 1902 by typhoid fever, at that time the scourge of Philadelphia, owing to its contaminated water and milk supplies.

It may be said that Frank Packard's medical career began when he entered, in 1887, the two-year course in the Biological Department of the University, which later developed into the premedical course of today. No degree was required in those days for enrollment in the Medical School, a high school certificate being all that was necessary. The Department of Biology had a distinguished faculty, with such eminent teachers and scientists as Cope, Ryder, Macfarlane and Horace Jayne, who taught cat anatomy and osteology, and Edgar

Fahs Smith, who later became Provost, in chemistry.

Dr. Packard's certificate was granted in 1889, and he entered the Medical Department in the class of 1892. At that time the course was for three years only, it not being extended to the full four years until my class of 1897. It was a legend of the time that both Fred and Frank were the gold medal men of their classes and had received the highest average marks ever obtained in the Medical School.

Shortly after graduation Frank Packard began an internship in the Children's Hospital, where he learned Otology from Dr. B. Alexander Randall, and then, in 1894, a two-year term as resident (it would now be called an internship) in the Pennsylvania Hospital, where he was connected until his death in 1950. Either before he began his Children's Hospital service, or between that and his start at the Pennsylvania Hospital, he served a short internship in the Johns Hopkins Hospital in Baltimore, where he would have been under the influence of Dr. John Noland Mackenzie, one of the American pioneers in laryngology, whose thesis on "The Massacre of the Tonsils" created world-wide discussion. I am inclined to think that this interlude occurred between the Children's and Pennsylvania Hospital appointments, as at that time only one resident was elected by the Managers of the latter institution every three months—four a year—and it was probably while waiting for his turn that he filled in the time in Baltimore. This was a common procedure in those days.

The intern's service was a general rotating one, with three months in the Mental Department, familiarly known as Kirkbride's. The Ear, Nose and Throat Department was not an active one, although headed by two distinguished specialists. Dr. George Harlan was Ophthalmologist and Otologist, and did what mastoid surgery came along, while Dr. Alexander MacCoy was Laryngologist, his work being largely confined to a few tonsillotomies (tonsillectomy had not yet been put in the books), and an occasional tracheotomy, the chief work being done in the O.P.D.

Immediately upon receiving his certificate for two years' service and the customary History of the Pennsylvania Hospital by Dr. Thomas G. Morton, Dr. Packard opened his office for private practice with Dr. John H. Gibbon, a fellow resident, joined the Out-Patient Staff on the Otological Service of Dr. Harlan, and became a quiz-master in therapeutics at the Medical School, the Professor being Dr. Horatio C. Wood, distinguished also as a neurologist, writer and orator. Here I first made Frank Packard's professional acquaintance, as I was a member of his first quiz class, and it was, I am sure, due to his careful teaching (for a quiz-master was a real teacher) that I successfully passed Dr. Wood's exacting oral examination.

His quiz-classes continued for a number of years, and about 1902, on Dr. Harlan's retirement, he became Surgeon to the Ear Department of the Pennsylvania Hospital. A few years later, when Dr. MacCoy retired also, the ear and the nose and throat services were united under his "chiefship," although they were still listed in the hospital catalogue as Out-Patient Service. During his long service as Chief and Consulting Otolaryngologist, the department, both in-patient and out-patient, reached a very high standard of efficiency and became one of the major services in the Hospital, where its wealth of material furnished splendid training facilities for many young practitioners and for the investigating of research problems.

I joined Dr. Packard's staff on finishing my internship, December 31st, 1901, and a few months later followed him to the Philadelphia Polyclinic and College for Graduates in Medicine when he became Professor of Otology there. The teaching there was entirely clinical in the outpatient department, and the course was of six weeks' duration. There was little surgery, but once a year a special week of instruction was given, during which some lectures in the surgical amphitheatre were included. Dr. B. Alexander Randall had been Dr. Packard's predecessor in the Chair, Dr. George C. Stout was a colleague, and Dr.

Walter Roberts his associate and successor when, a few years later, he took the place of Dr. Eugene L. Vansant as Professor of Laryngology. Here his colleagues were Dr. Joseph Gibb and Dr. Arthur W. Watson (recently deceased). At this time, also, he served as Dean of the Polyclinic School.

In 1903 Dr. Packard was elected a fellow of both the American Otological Society and of the American Laryngological Association, the first of its kind in the world. He was one of the youngest men admitted to fellowship, and both elections took place during the same week. He was also one of the organizers of the American Laryngological, Rhinological and Otological Society (the Triological), a group organized for the purpose of encouraging the younger specialists who had not yet qualified for admission to the so-called senior societies whose membership was, and is, limited to one hundred, mostly teachers, writers and research workers. The Triological Society has prospered greatly, and now numbers nearly four hundred, including all the eminent specialists in this country and Canada. In these days Dr. Packard took an active part in the proceedings of these organizations, and presented a number of papers, although he was never a prolific writer and soon his contributions were limited to those of historical interest. In 1909 he published his text book on Diseases of the Ear, Nose and Throat.

He continued in his Polyclinic service for about ten years, and thereafter confined his hospital work entirely to the Pennsylvania Hospital until his retirement from the active staff at the statutory age of sixty-five, and then continued as Consultant.

In 1907, following the American visit of Professor Gustave Killian of Freiburg, who was one of the pioneers in bronchoscopy, he became, with Dr. Emma Musson of the Woman's Medical College of Pennsylvania, one of the two Philadelphians to take up this subspecialty, although Chevalier Jackson, then in Pittsburgh, had done much pioneering work in this line, and was probably, even then, the superior of Killian or any of the Europeans, and certainly of any American. Dr. Packard was the first in Philadelphia to use the Killian, and later the Lynch modification, suspension apparatus for direct laryngoscopy and bronchoscopy.

When the Graduate School of Medicine was established in 1919, Dr. Packard became one of the Professors of Otology, and although outpatient teaching in the Pennsylvania Hospital was (and still is under Dr. Edward Campbell) carried on there, he took no active part, the work being done by staff members. He was also at various times active otolaryngologist or consultant to the Bryn Mawr, Children's and Chestnut Hill Hospitals, the Pennsylvania Institution for the Deaf, the Eastern State Penitentiary, and the State Asylum for the Insane at Norristown.

He served for years from 1901 as editor of the *American Journal of the Medical Sciences*, and in 1917 and succeeding years as editor of the *Annals of Medical History*. He received the honorary degree of LL.D. from his Alma Mater in 1939, and the Newcomb Award of the American Laryngological Association in 1942 for his historical researches and writings. In 1931 he was president of the American Otological Society, and in 1931–33 he served as president of the College of Physicians of Philadelphia, and thereafter continued on the Board of Censors of the College.

Military Service: In the Spring of 1898, on the outbreak of the war with Spain, Dr. Packard became First Lieutenant and Assistant Surgeon of the Second Regiment, Pennsylvania Volunteer Infantry, a National Guard Regiment with a splendid Civil War Record, at that time under the command of Colonel Henry Deckert. The Second Regiment was assigned to duty guarding the duPont works near Wilmington, and did not leave the country, and most fortunately did not suffer from the terrible morbidity and mortality from typhoid fever that prevailed in many of the more southern camps. When the National Guard was reorganized in 1901, he became Regimental Surgeon with the rank of Major, and partici-

pated in the annual summer encampments at Mt. Gretna, Perkasie and Gettysburg.

In 1917 he was a First Lieutenant, M.C. Reserve, and when the Pennsylvania Hospital Red Cross Hospital was organized by Dr. Richard Harte, he became Otolaryngologist with the rank of Captain. This unit was designated Base Hospital #10, American Expeditionary Forces, and sailed for France May 18th, 1917, proceeding eventually to Le Tréport on the channel coast of France, where it replaced Base Hospital #16, B.E.F., and so came under British command with this title. The unit eventually returned to American command and resumed its former designation. There being little or no otolaryngology in this hospital, Captain Packard helped out in keeping records, taking histories, and lecturing on French history to hospital personnel. Soon, however, he went to the Front with a surgical team commanded by Dr. Charles F. Mitchell, where he spent five months of hard work as anaesthetist under disheartening battle-line conditions. In October, 1918, with the rank of Major, he became Chief Centre Consultant in Otolaryngology for the district of Paris, and was honorably discharged in January, 1919, as Lieutenant Colonel.

Remarks. Robert J. Hunter, M.D.

Like all Dr. Coates' papers this one is concise, accurate and written in simple style. It gives us a clear cut account of the steady and rapid progress of Dr. Packard's career. Having become chief of the nose and throat service at the Pennsylvania Hospital at the age of thirty-two, his fame grew steadily. He developed a large private practice among the elite families of Philadelphia. One heard his name mentioned on every side as a court of last resort for ear, nose and throat work in the earlier days of his career and many faithful patients remained among his clientele until the last, even though his main interest had shifted to Medical History.

I first met Dr. Packard in 1918, when on my return from World War I, I worked for a short time at the Pennsylvania Hospital Ear, Nose and Throat Clinic. He had turned this over to assistants so I really saw little of his professional work. It was about this time that Dr. Packard began to devote more attention to History of Medicine and some of his associates came more and more into the public eye in the line of nose and throat work. We must view his attainments in the light of the spirit and knowledge of his time. When he began in the speciality of ear, nose and throat work, American text books covered sinus diseases in about four pages. The subspecialties of bronchoscopy, plastic surgery and allergy, have all been created one might almost say, since he began to practice. The same thought applies to his work in the field of history. In American medicine he was one of the men who developed the medical public's consciousness of Medical History and made it possible for the full time specialists in medical history to develop.

I would say that few men have the honor of making a great success in two fields of endeavor and having their fellow colleagues recognize their achievements in a commemorative meeting such as we are having tonight.

When he was 59 years old I became interested in the history of The Philadelphia General Hospital (Old Blockley). It was in this connection that I had my most intimate contacts with Dr. Packard. When we had the "Two Hundredth Anniversary of the building of the Philadelphia Almshouse" in 1932, Dr. Packard was appointed to represent the Pennsylvania Hospital and attended the ceremonies in that capacity. The last letter I received from Dr. Packard was one congratulating us on our success and regretting his inability to attend the Osler Centenary Celebration at Blockley. At the same time he requested reprints of the papers and very kindly sent us three of his Osler papers. Dr. Packard was at his best when displaying the treasures of the Library at the Pennsylvania Hospital. I shall always recall him there. Nothing could be more appropriate than that this commemorative meeting be made a part of the Two Hundredth Anniversary of the Founding of the Pennsylvania Hospital.

Dr. Packard As a Student of Medical History and Especially That of the Pennsylvania Hospital.

Edward B. Krumbhaar, M.D.

It is highly appropriate to link a Francis R. Packard Memorial Meeting with one that has to do with his favorite institution, The Pennsylvania Hospital, which this year celebrates its 200th anniversary. This hospital has been unusually fortunate in its chroniclers—starting with Benjamin Franklin's "Some Account" in 1754, followed by Malin's brief survey a generation later, George B. Wood's Centennial Address in 1851, J. Forsyth Meigs' continuation of the story 25 years later, T. G. Morton's very full factual account of 1895, and finally Dr. Packard's "Some Account" of 1938—one of the best. His spirit will long pervade the old library where he labored so lovingly and inspired so many of the younger men with the hospital's esprit de corps and traditions.

Dr. Packard was connected with the hospital practically throughout his life—at first indirectly through his father and older brother, Fred, who were both on its staff, and then as Intern (Resident), as a member of its staff and finally as Keeper of the Archives, a term selected by him for a position that gave free play to his bibliophilic and historical leanings. It is too bad that he is not still with us to enrich the Hospital's celebration this year! His "Some Account of the Pennsylvania Hospital from Its First Rise to the Beginning of 1938," prepared in the same format and typography as Franklin's "Some Account" shows his historical style and substance at its best. No one who loves the hospital should be without a copy.

Packard, Garrison and Sigerist (during his short stay here) were clearly the most eminent American medical historians of recent times, the last named being the only professional historian of the three. While all made noteworthy published contributions (Packard's, perhaps less so than the others) he was the most heavily endowed of the three with several important qualifications for a historian—especially a phenomenal memory. This gave full play to his ability, like Osler's, to converse extemporaneously and brilliantly on topics near to his heart. Another necessary attribute for a successful historian—in fact, for success in almost any walk of life—was his enthusiasm for his subject. Indeed, this was such an integral part of his intellectual make-up that it may even be taken as the explanation of some of his limitations as a writer on medical history. About subjects that he was interested in he wrote well and interestingly. Those that did not interest him he let severely alone—a convenient method, but one that is apt to produce unbalanced results. For instance, his "History of Medicine in the United States," his most important literary effort, is, as he himself pointed out in its Preface (for no one was more honest than the subject of our eulogies tonight), a series of essays and compilations and not a continuous historical work, such as Garrison's. One is prompted to ask—Why then was it not called "Essays on the History, etc."? You will recall that Garrison, erring at the other extreme and laboring under German influence, called his book "An Introduction to the History . . ."

In Mr. McDaniel's memoir in the *Bulletin of the History of Medicine* (Jan.-Feb., 1951), quite the best that has been written about Dr. Packard, a penetrating explanation of his tendency to dilettantism in his written work is offered. In support of Packard's own explanation—the "avocation formula"—it must be remembered that through most of his life, he was an extremely busy practitioner of his specialty. One can hardly imagine, for instance, that, in order to acquire a wider and sounder knowledge of Arabic medicine he would undertake to learn Arabic, as Sigerist did under similar circumstances. Indeed it would be hard to picture him really wanting to learn any more about Arabic medicine merely to round out his historical equipment.

Continuing consideration of Dr. Packard's qualifications as a historian, in addition to his prodigious memory and his enthusiasm for the subject, there should be added his instinct for hitting on an entertaining subject, his unerring

sense of values in selecting the best material to adorn it, his flair for the quaint and unexpected, and a fullness of the knowledge that comes from voracious reading. These traits, too, are of the kind that make a good speaker or conversationalist and he gave freely of them when intrigued or in the humor. A good example of his wide and accurate memory is seen in his historical lectures to the personnel of Base Hospital 10, during an enforced period of idleness in World War I. Responding to the desire that our personnel be entertained, he gave a brilliant and accurate series of lectures on the history of that part of France that was near our hospital in Normandy, with no reference library available for facts, names and dates.

Like most authors and editors, Dr. Packard was often irked by the minutiae of preparing for publication. Errors, never entirely absent in any sizeable publication, were a little more frequent than one expects from a meticulous fact-checker or proof-reader; and it is said that, like Virchow, who edited a famous *Archiv* for many years, when an article was once accepted by him for the *Annals of Medical History*, he let any blame for its shortcomings fall on the head of the author with entire complacency. Nevertheless, both the *Annals* and *Virchows Archiv* were in the top rank in their respective fields.

His editorship of the *Annals of Medical History*, which he conducted so conspicuously throughout its entire existence of 25 years, is, I quite agree, one of his chief contributions to medical history. Its continued success was undoubtedly favored by the happy collaboration of editor and the owner-publisher, P. B. Hoeber. This picturesque figure, whom Dr. Packard so warmly praised in his Foreword to the Cumulated Index of the *Annals*, published in 1946, combined a glamorous setting for his journal in his New York office, with a prodigious energy in selling his wares, the *Annals* included, to participants in medical meetings throughout the country. A visit to Hoeber sitting at a huge desk in his office, always with a cigar in his mouth, which was more often dead than alive, surrounded by push buttons, which were constantly in use to summon minions to produce this or that material, was very apt to suggest the oriental despot at home among his slaves. Not that he was in the least despotic, however; on the contrary, he was so friendly and helpful that he naturally drew to him the New Yorkers or out of town visitors who were interested in medical history. Among them would be found most of those who led the renewed interest in medical history in this country—Garrison, Cushing, Ruhräh, Crummer, Clendening, Riesman, Streeter and probably most of the members of the Charaka Club. No wonder he and Packard made an excellent team! Packard's extensive knowledge of the subject and his wide international reputation made it easy for him to get eminent names on his Editorial Board, which helped in turn to establish a flow of historical articles from ever widening circles.

Mr. McDaniel lists 7 historical books, of which Dr. Packard was author or editor and translator, and 97 historical articles on numerous phases of our field. Of the 7 books, the "History of Medicine in the United States" and "Some Account of the Pennsylvania Hospital" were all his own. The other 5, on "The Gold Headed Cane," "The School of Salernum," Ambroise Paré, Guy Patin, and Base Hospital 10, though either written in collaboration, or containing mostly text reprinting or translation, were made truly his by the delightful prefaces or notes from his pen. Five of the 7 were published in the decade 1915–1925. As one might expect, the greatest number of the articles (about $\frac{1}{2}$) appeared in the *Annals of Medical History*. Our *Transactions & Studies* appear in the list 7 times, the remainder of the list being distributed through many journals from 1893 to 1949. During these 51 years, there were but 14 that did not see the appearance in print of some historical article from his pen, and 3 of these 14 were the war years 1916–1918. Compensation for these 3 was prompt, however, 9 articles appearing in 1919. Incidentally, without attempting to gild the lily, it would seem proper to add to

McDaniel's list a footnote on the numerous biographical sketches signed "Francis R. Packard" in Kelly and Burrage's "American Medical Biographies."

In addition to occasional papers, obituaries, etc., Dr. Packard's interests revolved chiefly, as far as American medicine is concerned, around the subjects that constituted the 15 chapters of his "History of Medicine in the United States" (1931): namely, aspects of colonial medical history, hospitals and medical schools, medicine during the Revolution, notable medical events and the beginnings of specialism. Abroad, he turned mostly to the British (17 times), whose sterling qualities were much admired by him, with the French as worthy followers (8 times). This is not the place, however, to consider even the more important of Dr. Packard's historical articles seriatim. Fortunately, this aspect has already been dealt with in Mr. McDaniel's memoir.

In this appraisal I have endeavored to be as frank as possible—the only way that Dr. Packard would have wanted. It sums up into a conclusion that he was so richly endowed by nature that, while writing and speaking as he chose, he could at the same time leave us a very valuable intellectual heritage. I cannot refrain also from invading Dr. Fraley's field to the extent of expressing my great admiration for his many vivid traits and personal charm. I have missed him a lot and shall long continue to do so. As Hamlet said long ago,

"He was a man, take him for all in all,
I shall not look upon his like again".

Remarks. W. B. McDaniel, 2d, PH.D.

An invitation to so remote a College official as the librarian to say a few words at a meeting commemorating the achievements and personality of a past-president argues, of course, a relationship of a high sort between the past-president and the College library. Dr. Packard was, indeed, an outstanding member of that glorious band of what we might call library-presidents; that is, presidents—such as Samuel Lewis, Weir Mitchell, John Ashhurst, Jr., W. W. Keen, and, if he will forgive me for bridging two worlds, the last speaker—whose vision, enterprise, and generosity made the highest ideals for the library the only respectable ones that could be held in their time.

When Dr. Packard joined the distinguished line of great library-presidents, in 1931, he had, like most of the others, served a lengthy and probably a hardy novitiate. For seven years (1908–1914) he had been a member of the Library Committee; for eight additional years (1920–1927), the Honorary Librarian. If this young man needed indoctrination, which is inconceivable, he was enrolled in a school well equipped to provide both logic and inspiration, with a faculty including, for instance, such dynamic, purposeful mentors as Weir Mitchell, F. P. Henry, W. W. Keen, Osler (at a distance but never out of touch)—and this country's first great professional medical librarian, Mr. Charles Perry Fisher. What these sturdy, resolute, homogeneous teams accomplished there is not time to relate here; but the story is on record, and a glorious chapter it is. Whatever the reasons were that brought the chapter to a close, there was a touching demonstration, at the end, of that deep sense of loyalty so characteristic of the man Francis R. Packard. One observer will never forget the look of inner, reflective sadness on Dr. Packard's face, a few years later, during the funeral services for Mr. Fisher. It is not often that one is privileged to witness such essential purity of human feeling.

At the end of his presidency, in 1933, Dr. Packard no longer had any direct official responsibility for the conduct of the library; but it remained, as it did with Osler, close to his heart, and all know that he bequeathed to it his splendid collection of medico-historical books. From 1934 until shortly before his death, Dr. Packard attended the Council meetings at the College with uncommon regularity; and almost as regularly honored the librarian with a visit of an hour or so preceding the meeting—seldom coming in empty handed, it may be observed. Doubtless knowing that Dr. Packard was likely to be there, others would drop in, the otherwise not notably reticent

librarian would retire into the background, and the fun would begin. At such times, you will readily believe, the librarian had no complaint about a librarian's lot being an unhappy one.

Dr. Packard's historical interests inevitably drew us of the library into sympathetic relationship, in a small way, with the work of this Section. As you know, he was chairman of the Section, 1913–1922, and again in 1936, thereafter serving on the Executive Committee for several years. It may be that the memories of several in this room would confirm the impression that interest among the Fellows in medical history was probably never more widespread than when the Ariel of S. 19th St. was lending his phenomenal memory, his learning, his enthusiasm, and his lively wit to the affairs of the Section. More than that, with such allies as Dr. Krumbhaar, Dr. Riesman, and Dr. Robertson, he instituted a series of annual students' nights that may well be regarded as the precursor of the Section's present annual medical history course for medical students, now receiving such favorable national attention.

That Dr. Packard's concern for those who must inherit the earth was bread cast upon the waters is no surprise, of course, to those familiar with the respect and affection returned for his unfailing helpfulness. Last Saturday the library received unexpectedly a letter which beautifully illustrates this aspect of his character. Mr. Lyman Butterfield, one of our younger scholars, whose forthcoming edition of the letters of Benjamin Rush promises to be one of the major literary events of the year, wrote, in part:

"Whether it is of any use to you or not, I am anxious to put on record my personal indebtedness to Dr. Packard as a medical historian. I vividly remember the warmth with which he welcomed my suggestion of an edition of Benjamin Rush's letters, and how he at once opened doors, made highly constructive suggestions, and generally put himself at the service of my project. All this was tremendously encouraging to me—a mere novice in this specialized field. I say nothing of the privilege of sharing his friendship during the too few years I knew him. Whoever loved medical history was Dr. Packard's friend."

Tonight is an April night, the season when, in the English-speaking world, at least, new life burgeons from the old. May we always gratefully, as we are doing tonight, recognize the good in our heritage—and beget, if we can, a better one.

Pathological Society of Philadelphia

PROCEEDINGS

N. S. Vol. 39: OCTOBER, 1950–May, 1951

Peter A. Herbut, *President*

Warner F. Sheldon, *Secretary*

October 12, 1950

SYMPOSIUM ON ADRENAL PATHOLOGY

ENDOCRINE AND CONNECTIVE TISSUE CELLULAR RESPONSES TO ADMINISTRATION OF A BACTERIAL PYROGEN. William F. Windle. (*Abstract 1, below*)

ADRENAL CORTICAL RELATIONSHIPS IN HEALTH AND DISEASE. William E. Ehrich. (*Abstract 2, below*)

ADRENOCORTICAL TUMORS. Karl E. Paschkis. (*Abstract 3, below*)

November 9, 1950

SYMPOSIUM ON ADENOMA OF THE BRONCHUS

CLINICAL MANIFESTATIONS. W. Emory Burnett. (*No abstract received*)

BRONCHOLOGIC ASPECTS. Louis H. Clerf. (*Abstract 4, below*)

ROENTGENOLOGIC ASPECTS. Russell Wigh. (*Abstract 5, below*)

PATHOLOGIC ASPECTS. Anthony L. Pietroluongo. (*Abstract 6, below*)

December 14, 1950

FATTY INFILTRATION OF THE LIVER: ITS RELATIONS TO TRANSMETHYLATION. J. A. Stekol. (*Abstract 7, below*)

CLEAVAGE AND DIFFERENTIATION IN CELLS LACKING CHROMOSOMES. Robert Briggs. (*No abstract received*)

IRRADIATION KERATOGENESIS IN METASTATIC SQUAMOUS CELL CARCINOMA. A. J. Donnelly. (*Abstract 8, below*)

January 11, 1951

RELATIONSHIP OF DURATION OF PRIMARY TUMOR GROWTH TO NUMBER OF METASTASES. Irving Zeidman. (*Abstract 9, below*)

DISTRIBUTION OF EMBOLIC TUMOR CELLS IN RELATION TO DISTRIBUTION OF RESULTING TUMORS. Morton McCutcheon. (*Abstract 10, below*)

INDUCTION OF ACCESSORY LIMBS IN THE NEWT WITH CARCINOGENIC SUBSTANCES. Charles Breedis. (*Abstract 11, below*)

February 8, 1951

MALIGNANT HEPATOMA IN INFANTS. J. H. Frank, B. F. Brooks, J. B. Arey, and A. DiGeorge. (*Abstract 12, below*)

INFECTIOUS HEPATITIS IN INFANCY AND EARLY CHILDHOOD. Irving J. Wolman, John D. Farquhar, and Joseph Stokes, Jr. (*Abstract 13, below*)

CAUSES OF FETAL AND NEONATAL DEATH. James B. Arey. (*Abstract 14, below*)

March 8, 1951

Annual Joint Meeting with Section on Clinical Pathology of the Philadelphia County Medical Society.

April 12, 1951

Slide seminar: UNUSUAL TUMORS OF THE BREAST. Clark E. Brown and John E. Hopkins.

May 10, 1951

INTRATHORACIC LESIONS SIMULATING CARCINOMA OF THE LUNG: TUMORS. A. Reynolds Crane. (*Abstract 15, below*); ACQUIRED LESIONS. Primitivo T. Cruz. (*Abstract 16, below*); CONGENITAL LESIONS. Allan D. Wallis. (*Abstract 17, below*)

Abstracts

Abstract 1

Endocrine and Connective Tissue Cellular Responses to Administration of a Bacterial Pyrogen.[1] William F. Windle. Physiological and histological studies were undertaken to learn the site of action of a new pyrogenic drug and the possibility of toxic reactions. This drug, Pyromen, is a highly purified nonprotein bacterial extract. Its toxicity is slight, the LD_{50} in mice being 75,000 to 100,000 gamma/Kg. Rabbits receiving massive doses exhibited no significant liver, kidney, intestinal or brain pathology. The marked pathology of the exhaustion phase of the general adaptation syndrome was not encountered but other more subtle reactions suggestive of increased output of pituitary ACTH secretion, and differing from changes accompanying physically induced fever, were encountered.

Events following Pyromen administration were studied in various species. A dose of 1 or 5 gamma/Kg. induced leucopenia and eosinopenia within one hour, reaching a low point in 4 hours, followed by lymphocytosis in the rat, cat, dog and human. An increased output of urinary, 17 ketosteroids in cats or corticoids in rabbits was not detected. Connective tissue mast cells of mice exhibited dispersion of their cytoplasmic granules within one hour. Controlled histological studies of all organs of rabbits revealed a panendocrine reaction to Pyromen, beginning in 12 to 24 hours and exhibiting nearly maximal effects in 10 days or less. This was manifested by vacuolation of cell cytoplasm in adrenal medulla and cortex, in pituitary chromophobes and basophils, and in cells of parathyroid and insular pancreas. The interstitial cells of the ovarian stroma of the rabbit underwent hypertrophy within 24 hours and became vacuolated. Prolonged Pyromen administration induced hyperactivity of lymphatic organs, resulting in proliferation of macrophages and lymphocytes, inducing hyperplasia (and even metaplasia with granulocyte production) in spleen. Vascularity was enhanced in most organs. Proliferation of indifferent connective tissue cells followed Pyromen administration. After spinal cord transection in dogs and cats, fibrous and glial scars appeared to be inhibited and a cellular field developed between the cut surfaces through which central neurons regenerated as in regenerating peripheral nerves.

[1] Aided by a grant from Baxter Laboratories, Inc., Morton Grove, Illinois.

Abstract 2

Adrenal Cortical Relationships in Health and Disease. Willliam E. Ehrich. The adrenals are part of the equipment which enables us to adapt ourselves to the kaleidoscopic changes of environment. Under favorable conditions they aid in recovery. Under adverse conditions they may give rise to diseases.

Exposure to stress is followed first by a "shock phase" which is a vascular phenomenon, and then a "counter-shock phase" which culminates in the outpouring of adrenal corticosterones. These affect the permeability of hyaluronate containing membranes, the mineral metabolism, and the sugar and protein metabolism. The action upon the protein metabolism manifests itself in loss of zymogen granules in pancreas and other glands and in destruction of lymphocytes and plasma cells. The latter proceeds to the purine and pyrimidine level. It appears to be designed to furnish the body with nucleoprotein split products for synthesis of new protein and with stimuli for phosphorylation necessary for enzymatic activity.

The diseases which may result from too little or too much response of the adrenals are known as diseases of adaptation or diseases of dyscorticism. They include the following:

- Acute:
  - Hypocorticism:
    - Waterhouse-Friederichsen syndrome
  - Hypercorticism:
    - "Anginosis" (Fein)
    - Certain cases of appendicitis

Focal necroses of pancreas
Symptomatic parotitis
Chronic:
Hypocorticism:
Asthenia
Status thymico-lymphaticus
Addison's disease
Hypercorticism:
Certain cases of hypertension
Certain cases of diabetes
Cushing's syndrome

Chronic hypocorticism manifests itself in atrophy (hypophysectomy, Simmonds' disease, use of cortisone) or destruction of the adrenals (tuberculosis, metastatic tumor). Chronic hypercorticism is characterized by hypertrophy (chronic stress due to drugs, infection, starvation, use of ACTH) or neoplasia (adenoma, carcinoma). The adrenals may be involved also in the so-called collagen diseases and in allergy.

Abstract 3

Adrenocortical Tumors. Karl E. Paschkis. The author presented adrenocortical tumors from the angle of the physiological action of adrenocortical hormones. The cortex secretes (a) steroids chiefly acting upon electrolyte and water metabolism: "salt hormone" (desoxycorticosterone); (b) steroids acting chiefly upon protein-and carbohydrate metabolism: "sugar hormones" (17-hydroxycorticosterone, cortisone); (c) androgenic 17-ketosteroids, which exert a protein anabolic action: N-hormones (17-ketosteroids); (d) estrogens. Cortical tumors may be highly anaplastic, secreting no hormones; manifestations are those of tumor growth itself. The hormone secreting tumors may secrete one or several of the above mentioned hormones. Excessive secretion of all hormones (Panhypercorticalism) causes Cushing's syndrome. Tumors secreting excessively only (or almost only) the androgenic 17-ketosteroids cause extreme virilism (adrenogenital syndrome) in adult women, no significant endocrine abnormalities in adult males, precocious puberty of the heterosexual virilizing type in girls, and macrogenitosomia precox in boys. Tumors secreting only an excess of sugar hormone cause diabetes (one recorded case); rare tumors secreting preponderately excessive estrogens cause some feminization in males. No instance of isolated over production of salt hormone is known.

Since intermediate forms occur of tumors secreting one type of hormone preponderately, but still an excess of others, the picture may be kaleidoscopic, and more complicated than this basic outline would suggest. The "functional picture" of a tumor case is in most respects indistinguishable from that resulting from diffuse, benign hyperplasia. Quantitative differences exist. In adrenogenital syndrome due to diffuse adrenocortical hyperplasia the 17-ketosteroid excretion usually does not exceed 100–150 mg per 24 hrs; in tumor cases it may be as high as 800 mg; a disproportionately high percentage of the 17-ketosteroids in tumor cases is dehydroisoandrosterone.

Different types of tumors as outlined above were illustrated by lantern slides.

Abstract 4

Adenoma of the Bronchus: Bronchologic Aspects. Louis H. Clerf.

From the bronchologist's standpoint adenoma of the bronchus presents several important problems. While the roentgenologist is aware of the presence of partial or complete bronchial obstruction, the cause is not always apparent. To the bronchologist the finding of a reddish or purplish mass, more or less sessile, and partially or completely blocking a bronchus is almost always diagnostic of adenoma. Carcinoma practically never appears as a nonulcerating, noninfiltrating lesion. Other benign tumors commonly do not exhibit the smooth, vascular appearance as exhibited by adenoma.

While no opinion can be given purely on the basis of gross microscopic appearances it is often with hesitancy that the bronchologist does a biopsy on adenoma, since these lesions are notoriously vascular and severe hemorrhage may occur. If he is prepared to cope with this emergency by application of a tampon or lung pack, the hazards are relatively insignificant. Since adenoma may be pedunculated one may

occasionally utilize forward grasping forceps to remove part of the tumor or by employing the tip of the bronchoscope as a corer a large mass may be secured.

It is impossible for the bronchologist to determine whether the lesion is entirely endobronchial or whether there is a portion of it outside the bronchus. Following removal of the endobronchial portion and allowing time for clearing of the pneumonitis which commonly results following complete obstruction of a bronchus tomographic studies may be helpful in determining whether residual tumor remains.

In the event that there is roentgen evidence of extrabronchial tumor or if on the basis of a bronchogram there is bronchiectasis distal to the endobronchial portion of the tumor the case usually resolves itself into a surgical problem.

In the purely endobronchial type of lesion bronchoscopic diathermy with forceps removal often is adequate in permanently removing and destroying the tumor itself.

In conclusion, adenoma of the bronchus although not a common tumor, constitutes a serious problem because of the occurrence of hemoptysis as a common symptom, pneumonitis or bronchiectasis distal to the point of obstruction, and the frequent association of an extrabronchial portion of tumor which cannot be controlled by endobronchial means and usually results in a compressive stenosis with increasing difficulties in drainage and increasing bronchiectasis. It would appear therefore that when a diagnosis of adenoma is made every effort should be made to determine whether the lesion can be reasonably controlled by endobronchial means or whether it constitutes a surgical problem and should be extirpated.

Abstract 5

ADENOMA OF THE BRONCHUS: ROENTGENOLOGIC ASPECTS. Russell Wigh.

The roentgenologic manifestations of bronchial adenoma are almost always due to the peripheral changes that occur secondary to the endobronchial neoplasm. In a review of the last 20 cases seen at Jefferson Medical College Hospital, not a single instance was noted in which an extrabronchial component of the neoplasm itself was recognizable. Rabin (in Golden's "Diagnostic Roentgenology") found only 2 cases among 40 in which the growth extended outward from the bronchus into the lung to produce a round opacity.

The prominent features seen are those of atelectasis and bronchiectasis. Large saccular bronchiectatic cavities or actual pulmonary excavation may be observed on plain roentgenograms. Bucky studies will demonstrate these latter changes more readily. When segments of lung smaller than a lobe collapse, on the postero-anterior projection the atelectatic segment may suggest a mass but the lateral roentgenogram demonstrates the true nature of the change. It is possible that at times the parenchymal collapse itself conceals an extrabronchial portion of the new growth.

Very rarely does the neoplasm lead to obstructive emphysema. Only one of our cases showed this feature and in a short period the obstruction became sufficiently occlusive to produce collapse.

Planigraphic and bronchographic studies are very helpful in outlining the neoplasms. It is surprising to find that many are not simple round or hemispheric tumors but that they may be quite flat and extend for 4 or 5 cm. along a bronchial wall.

Abstract 6

ADENOMA OF THE BRONCHUS: PATHOLOGICAL ASPECTS. Anthony L. Pietroluongo.

The pathological aspects of bronchial adenoma are of a dual nature. There are those concerning the tumor directly and others which result from bronchial obstruction followed by lung infection. The importance of the latter changes is acknowledged by all. However, there is a difference of opinion regarding the neoplasm itself, particularly insofar as its malignant potentialities are concerned.

The morphological appraisal of bronchial adenoma is not sufficient to predict its ultimate

behavior. In a survey of the material at Temple University Hospital this fact was impressive. There were cases of the carcinoid type which demonstrated local invasion, lymphatic and vascular permeation as well as two instances of distant metastases. Yet, when the original biopsy sections and those of the metastatic deposits were compared with each other and with material from non-aggressive adenomas, there were no significant differences.

Again illustrated is the important fact that for the proper assessment of a neoplasm other criteria as well as morphology must be employed. Due regard must be given to the clinical aspects as well as biologic behavior. When applying this overall evaluation there are still some tumors which cannot be placed neatly into either a benign or malignant compartment. They possess some features of each category which have to be considered for proper management of such cases. Bronchial adenoma is one of this group.

Abstract 7

FATTY INFILTRATION OF THE LIVER: ITS RELATION TO TRANSMETHYLATION. J. A. Stekol.

The process of transmethylation is defined as the transfer of the intact methyl groups of methionine and choline (and other metabolites which contain the "labile methyl" group) to other metabolites in the animal body. This process is of vital importance in relation to synthesis of choline *in vivo*, and hence to the metabolism and transport of lipids in the liver. Fatty infiltration of the liver was related to the availability of the lipotropic factors in the diet, namely methionine and choline. Until recently, it was believed that the "labile methyl" group of either choline or methionine cannot be synthesized in the animal body, and it had to be supplied in the diet either as methionine or choline or related substances. Work in this laboratory has shown that in animals the "labile methyl" group of either choline or methionine can be synthesized in total absence of these groups from the diet of the animals. It has been shown that vitamin B_{12} and folic acid are required in the diet to enable the animal to grow and synthesize methionine in complete absence of methionine in the diet. Confirmation of the synthesis of the labile methyl group *in vivo* has also been obtained by the use of radioactive glycine, formic acid, serine, methanol, and formaldehyde. The carbons of these metabolites served as the precursors of the labile methyl group of choline and methionine *in vivo*. In view of the relationship of vitamin B_{12} and folic acid to the synthesis of these labile methyl groups, the metabolic importance of vitamin B_{12} and folic acid to fatty infiltration in the liver cannot be overemphasized. Much more work is necessary to elucidate precisely the mechanisms in which these two vitamins are apparently intimately involved.

Abstract 8

IRRADIATION KERATOGENESIS IN METASTATIC SQUAMOUS CELL CARCINOMA. A. J. Donnelly.

Morphologic differentiation of stratified squamous epithelial cells is characterized by the differences seen in the various strata of cells in the epidermis and stratified squamous mucosa where progression is from the undifferentiated germinal layer to the end stage of complete morphologic differentiation, the keratinized squames. One of the characteristics of squamous cell carcinoma is the failure of the malignant cells to differentiate completely in the balanced normal rate. Ionizing radiations of X-ray or radium are effective in treating squamous cell carcinomas because one of the activities of such radiations is to enhance the natural tendencies of the neoplastic squamous cells to complete their life cycles to keratinization in which state they are sterile or incapable of further mitotic division. This effect of ionizing radiations is not their only means of therapeutic activity but would seem to be very important as judged by studies of nodes containing metastatic squamous cell carcinoma after exposure to relatively high doses of such radiations. These studies reveal that the metastatic carcinoma may be converted into a mass of apparently sterile keratinized cellular debris.

The degree of radiation keratogenesis varies greatly and is apparently dependent on the dose of radiation delivered as well as on the amount of natural tendency to keratinization inherent in the tumor.

A rare instance of complete keratogenesis has been found in a lymph node containing metastatic squamous cell carcinoma not treated by irradiation. This suggests that factors other than irradiation may be capable of inducing the change and such factors when discovered may greatly increase the beneficial effects of irradiation as used in treating squamous cell carcinoma.

Abstract 9

Relationship of Duration of Primary Tumor Growth to Number of Metastases. Irving Zeidman.

As recently reported, the number of metastases increases the longer a primary cancer is present in the host. Is this increase with time the result of successive releases of embolic cells, or is it due to the escape of tumor emboli of different sizes in a single shower? To test the hypothesis that emboli escape at different times, experiments were planned, using transplants of fibrosarcoma 241 in C57 black mice. This tumor regularly produces spontaneous pulmonary metastasis. Subcutaneous implants were removed at intervals, and the mice were sacrificed several weeks later. Of mice that had borne primary tumors for 11 to 12 days, about 50 percent were found to have pulmonary metastases; therefore 11 to 12 days was assumed to be the time of initial release of emboli. In subsequent experiments, the implants were removed 11 to 12 days after inoculation in one series of mice, and after 16 days in another series. All mice were sacrificed 32 days after inoculation. Significantly more metastases were found in those mice that had borne the tumor for the longer time. It is therefore concluded that the increasing number of metastases with time is dependent upon successive releases of emboli rather than upon a single shower of emboli from the primary tumor.

Abstract 10

Distribution of Embolic Tumor Cells in Relation to Distribution of Resulting Tumors. Morton McCutcheon.

The laws governing metastases of malignant tumors no longer need be regarded as mysterious or inaccessible to investigation. The long known differences in distribution of secondary tumors, their conspicuously greater frequency in adrenals and kidneys, their comparative scarceness in muscle, spleen, and thyroid, is explainable by the mechanics of circulation rather than by any peculiarities of the organs themselves. This mechanical hypothesis, obviating the "soil hypothesis", is that the number of secondary tumors arising in any organ is dependent on the number of tumor emboli that reach it.

The validity of this mechanical explanation of metastasis was tested by injecting cell suspensions of the Brown-Pearce tumor into the left cardiac ventricle of rabbits. Half the animals were immediately sacrificed, and the distribution of tumor cells (specially marked) ascertained in microscopic sections. The other rabbits were allowed to survive long enough for tumors to develop and were then sacrificed and the distribution of tumors ascertained. Kidneys, stomach, adrenals, eyes, diaphragm, pituitary, spleen, thyroid, and testes were involved in descending frequency. When listed according to number of emboli, the order was essentially the same. This result supports the mechanical hypothesis that metastatic tumors are numerically proportional to the tumor emboli that reach the various organs.

Abstract 11

Induction of Accessory Limbs in the Newt with Carcinogenic Substances. Charles Breedis.

Attempts were made to induce neoplasia in the forelimb of adult *Triturus viridescens* by means of carcinogens. Certain substances, notably carcinogenic tar, induced the formation of accessory limbs and limb parts when injected into the tissues of the forelimb. These growths arose from the site of injection after

50 to 100 days, grew rapidly at first, and ceased growing at approximately 200 days. They varied in complexity from complete reduplications of distal portions of the fore limb to digit-like and conical projections, and showed a high degree of tissue organization; in fact, some had the appearance and function of normal limbs. Attempts to transplant the growths to other parts of the same newt or to other newts were unsuccessful.

Malignant neoplasms occurred in 2 animals, both of which had received methylcholanthrene in olive oil. One tumor arose as a disorganized mass of sarcomatous tissue, the other as a sarcoma at the base of an accessory limb. Both were readily transplantable to other *T. viridescens*.

These findings indicate that methylcholanthrene, known to be carcinogenic for mammals, can also be carcinogenic for a cold-blooded vertebrate. So far as is known, this is the first instance of successful chemical induction of neoplasia in a cold-blooded animal. These experiments further suggest that some carcinogens are capable of inducing highly organized growth as well as neoplasia.

Abstract 12

Malignant Hepatoma in Infants. J. H. Frank, B. F. Brooks, J. B. Arey, and A. DiGeorge.

Two cases in male infants are described. The first, seventeen months old was admitted to Woman's Medical College Hospital and a mass in the left lobe of the liver was resected. A metastasis in the omentum was also removed. The tumor recurred in the right lobe and metastasis developed in both lungs. The child died fifty one days after the diagnosis had been established and an autopsy was performed.

The second, five and a half weeks, had an enlarged liver from birth. Exploratory laparotomy demonstrated a large inoperable mass in the right lobe. The child died eleven weeks later and was autopsied. In addition to the tumor of the liver, there was also found a metastasis in the left thalamus.

The presenting symptom in each case was abdominal mass. Anemia, fever and emaciation follow. In histologic structure, the tumors are comparable showing fairly well differentiated liver tissue. One appears to be largely of liver cell origin. The other includes neoplastic ductal elements. Their morphology suggests a development from embryonal rests.

Abstract 13

Infectious Hepatitis in Infancy and Early Childhood. Irving J. Wolman, John D. Farquhar, and Joseph Stokes, Jr.

A series of infants have been studied who exhibited signs of parenchymal liver disease with onset in the immediate postnatal period. These infants are thought to have had viral hepatitis of the IH or SH strains of virus. The pathologic findings in six of these who died of the disorder were similar to those described in older children and adults with viral hepatitis, though certain peculiar and apparently significant morphologic changes were seen in their livers. The most distinctive feature was the presence of unusually large and multinucleated parenchymal cells, sometimes containing large fat vacuoles. Cells of this type were demonstrated in nearly every fatal case. All children who died have come to autopsy since 1940, coincident with the presence of viral hepatitis in the civilian population. No similar instances were encountered in the autopsy experience of this hospital in the preceding 10 years. SH hepatitis virus was transmitted to human volunteers by parenteral injection from the blood of one of the infants who died, and also from his mother.

Abstract 14

Causes of Fetal and Neonatal Death. James B. Arey.

The material for the present study consists of the consecutive autopsy records of 35 nonmacerated fetuses and 102 liveborn infants dying during the first month of extrauterine life on the Tulane Service of the Charity Hospital of Louisiana at New Orleans. Macerated

fetuses or fetuses and infants weighing less than 500 Grams were excluded.

An adequate anatomic cause of death was demonstrated in 109 fetuses and infants, i.e., in 87 (85%) of the liveborn infants and in 22 (62%) of the stillborn fetuses. The anatomic causes of death are listed in *Table 1.*

Intrauterine anoxia, as evidenced by excessive aspiration of amniotic debris was the single leading cause of death, accounting for 23 (16%) of the fetal and neonatal deaths. Small amounts of amniotic debris were found in the lungs of most fetuses and infants dying in the early neonatal period, but there is good evidence to indicate that the presence of large amounts of such material within the lungs is evidence of fetal anoxia. It is felt that the majority of these fetuses and infants die as a result of cerebral damage and not primarily as a result of the inhalation of amniotic debris.

TABLE I.
ANATOMIC CAUSES OF DEATH

Undetermined	28
Fetal anoxia (aspiration of amniotic debris)	23
Intrapulmonary hyaline membrane	15
Congenital Anomalies	14
Intraventricular hemorrhage	11
Bronchopneumonia	10
Congenital Syphilis	9
Miscellaneous	27
Total	137

An intrapulmonary hyaline membrane was the second leading cause of death, accounting for the death of 15 liveborn infants. No examples of an intrapulmonary hyaline membrane were encountered in the group of stillborn fetuses. The clinical behaviour of patients suffering from an intrapulmonary hyaline membrane is often so characteristic that the correct pathologic diagnosis can be suggested antemortem; positive diagnosis, however, is dependent upon histologic examination of the lungs at the time of autopsy. Although many authors believe that such intrapulmonary hyaline membranes are composed of aspirated amniotic sac contents and vernix caseosa, the evidence for this is inconclusive. On purely theoretical grounds there is much to support the concept that such membranes are at least in part the result of vascular damage and increased capillary fragility.

Major congenital anomalies accounted for 10% of the total fetal and neonatal mortality, and lethal or potentially lethal congenital anomalies were present in 3 additional fetuses and infants as a contributory cause of death. Minor congenital anomalies were often present in the absence of any major anomaly. Many of these minor anomalies were of academic interest only, but a few of them, such as anomalies of the renal pelvis and ureter, ovarian hypoplasia, and an anomalous course of the right subclavian artery, may assume clinical significance somewhat later in life.

Intraventricular hemorrhage was responsible for the death of 11 premature liveborn infants. An obstetrical history indicative of a traumatic delivery was not recorded for the majority of these infants, and the fact that such hemorrhages occur far more frequently in premature than in full-term infants suggests that certain factors inherent in premature infants play an important role in their pathogenesis.

Bronchopneumonia was held responsible for the death of 9 premature infants and 1 full term infant, and was present as a contributory factor in 26 additional liveborn infants and in 3 stillborn fetuses. Among the 36 liveborn infants with bronchopneumonia 26 lived less than 72 hours. The diagnosis of bronchopneumonia in infants dying in the early neonatal period is dependent upon histologic examination of the lungs; histologic sections should be prepared from all lobes of the lungs, as the inflammatory infiltrate may be present in only one of multiple sections.

Congenital syphilis was responsible for the death of 8 liveborn premature infants and one full-term fetus. Other causes of death in the remainder of the series included such miscellaneous lesions as dural tears, thrombosis of dural sinuses, meningitis, omphalitis, erythroblastosis fetalis, intrapulmonary hemorrhage, and kernicterus.

The importance of multiple histologic sec-

tions, especially of the lungs, careful examination of the fixed brain, and of correlation of the pathologic findings with the clinical record is emphasized.

Abstract 15

INTRATHORACIC LESIONS SIMULATING CARCINOMA OF THE LUNG: TUMORS. A. Reynolds Crane.

Increasing periodic health surveys, including roentgenograms of the chest, are bringing before the thoracic surgeon greater numbers of benign as well as malignant lesions. The differential diagnosis of solitary lesions on x-ray and clinical grounds is extremely difficult. The dictum of watching the course of a lesion is not to be condoned. If a diagnosis cannot be established on clinical grounds thoracotomy should be done promptly. Five neoplastic lesions of benign nature are presented.

1.) Solitary localized fibrous pleural mesothelioma occurring in a 69 year old white male. Successful surgical removal.

2.) Hemartoma of mixed cartilage and epithelial type occurring in a 47 year old white male. Successful surgical removal.

3.) Neurilemoma of intercostal nerve in a 38 year old white male. Radiologic lesion identical with previous 2 cases. Successful surgical removal.

4.) Thymic Rest (Thymoma) of left upper lobe of lung in 19 year old white female with history of marked fatigue and lassitude. Successful surgical removal with relief of symptoms of myesthenia.

5.) Pulmonary alveolar adenomatosis involving the right lower lobe only in a 65 year old white female. Lobectomy with no recurrence in 2 years.

Abstract 16

INTRATHORACIC LESIONS SIMULATING CARCINOMA OF THE LUNG: ACQUIRED LESIONS. Primitivo T. Cruz.

The surgical records of the Ayer Laboratory of the Pennsylvania Hospital from January 1, 1931 to December 31, 1950, were reviewed and a table of all acquired lesions in the thoracic cavity which may simulate bronchiogenic carcinoma was made. Four of the more unusual cases found were presented and discussed.

Case No. I was a case of lipoid pneumonia, adult type (Paraffinoma), in a 59 year old white male which was diagnosed clinically, roentgenologically, bronchoscopically, and even in gross pathology as a case of bronchiogenic carcinoma of the right middle lobe. The patient was symptom free. He died during the course of operation.

Case No. II was a 50 year old white female admitted for slight hemoptysis and chronic cough. Chest x-ray, bronchoscopic examination and one positive bronchial smear led to a diagnosis of carcinoma of the left lung. A left pneumonectomy was done, and the pathological diagnosis was tracheopathia osteoplastica. The patient recovered.

Case No. III was a case of an aspirated tooth in the right lower main bronchus. The patient (a 40 year old white female) came in because of cough, back pain, loss of weight, night fever and sweats. Chest x-ray was suggestive of a tumor mass in the right hilar area, but bronchoscopic examination revealed findings more in favor of inflammation. The patient underwent a right pneumonectomy and recovered.

Case No. IV was a 50 year old white male admitted for paroxysmal cough and slight hemoptysis. Radiological studies and bronchoscopic examination revealed findings suggestive of carcinoma of the right lung. A right pneumonectomy was done. Recovery was uneventful. Pathological diagnosis was bronchiolithiasis of the right main bronchus.

Abstract 17

INTRATHORACIC LESIONS SIMULATING CARCINOMA OF THE LUNG: CONGENITAL LESIONS. Allan D. Wallis.

Four cases are described. Of two mediastinal teratomas, one was of unusually large size (18 cm.) and the other had leaked into lung tissue causing a localized lipoid pneumonitis. A congenital pulmonary cyst gave rise to re-

current expectoration of large amounts of mucoid material. In a discussion of the origin of congenital cysts of the lung evidence is quoted which indicates that the bronchial tree continues to branch, with the formation of new ducts and alveoli, until the age of 7. A case of multiple pulmonary arteriovenous fistulae is reported, complicated by numerous arterial communications between the right lower lobe and the chest wall and diaphragm. The distinction between arteriovenous anastomosis and hemangioma is emphasized.

OFFICERS

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Changes in Membership

New Members

	Date of Election		Date of Election
Velat, Charles A.	11/ 9/50	Hunter, Albert L.	2/ 8/51
Harvey, J. G. Klemm	11/ 9/50	Abbiss, Joseph W.	4/12/51
Perlmutter, Henry J.	11/ 9/50	Bennett, Webster	4/12/51
Old, William J.	11/ 9/50	Brody, Henry	4/12/51
Crane, A. Peter	11/ 9/50	Figueiredo, Marco	4/12/51
Weller, Russell W.	11/ 9/50	Walker, Russel	4/12/51
McDonnell, William V.	11/ 9/50	Maniglia, Rosario	5/10/51
Palladino, Vincent S.	12/14/50	Koiwai, Eichi Karl	5/10/51
Faulconer, Robert J.	12/14/50	Tanner, Leonard M.	5/10/51
Mora, George J.	12/14/50	Haentze, Frederick E.	5/10/51
Jernstrom, Paul H.	12/14/50	Rose, S. Brandt	5/10/51

Resignations

Irey, Nelson (1950)

Deaths

Cohen, A. J. (1949)
Dorrance, G. M. (1949)
Eshner, A. A. (1949)
Forman, Horace J. (1949)
Forster, George B. (1949)
McKee, James H. (1950)

TRANSACTIONS & STUDIES

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The Adrenals in Health and Disease*

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I. Introduction

IT IS indeed a great honor for me to have been selected by the College of Physicians of Philadelphia as the recipient of the Alvarenga Award for the year 1951. I gratefully accept this honor in the spirit of the man whose keen interest in the advancement of medical science prompted its initiation. In so doing, I should like to recall those young men whose association I have valued so dearly during the past several years, and without whose whole-hearted collaboration I could not have undertaken the investigation for which this award has been made. I should particularly like to mention Dr. Peter H. Forsham, Dr. Thomas F. Frawley and Dr. D. Laurence Wilson, since all three have departed from my laboratory this year for distinguished academic appointments elsewhere.

Historically, Addison was the first to appreciate the importance and the essential nature of the adrenal glands. In 1855 in his classical description of the syndrome which now bears his name he made the following modest statement (1), which is undoubtedly more appropriate and better appreciated today than at any period during the intervening one hundred years!

"It will hardly be disputed that at the present moment, the functions of the supra-renal capsules, and the influence they exercise in the general economy, are almost or altogether unknown. The large supply of blood which they receive from three separate sources; their numerous nerves, derived immediately from the semilunar ganglia and solar plexus; their early development in the foetus; their unimpaired integrity to the latest period of life; and their peculiar gland-like structure; all point to the performance of some important office: nevertheless, beyond an ill-defined impression, founded on a consideration of their ultimate organization, that, in common with the spleen, thymus and thyroid body, they in some way or other minister to the elaboration of the blood, I am not aware that any modern authority has ventured to assign to them any special function or influence whatever. To the physiologist and to the scientific anatomist, therefore, they continue to be objects of deep interest, and doubtless both the physiologist and anatomist will be inclined to welcome, and regard with indulgence, the smallest contribution calculated to open out any new source of inquiry respecting them. . . . The leading and characteristic features of the morbid state to which I would direct attention, are, anaemia, general languor and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of colour in the skin, occurring in connexion with a diseased condition of the 'supra-renal capsules.' "

Brown-Séquard (2) in the following year (1856) demonstrated the lethal effect of removing both adrenals from rabbits. Following the identification of the characteristic staining qualities of the adrenal medulla by Vulpian (3) in the same year and the ultimate isolation and identification of epinephrine by Takamine (4) and Aldrich (5) in 1901, it was demonstrated that, although this substance elicited profound physiological effects in the intact organism, it was not essential for life. Cannon's "emergency theory of adrenal function" (6), however, clearly suggested the importance of the medullary secretion in permitting man to make the immediate and fine adjustments needed to meet a constantly changing environment and thus the stage was set for Selye (7) to point out the integrated role played by the medulla and cortex in the early and late adaptation to stress while the exact nature of adrenal cortical action was still far from being defined. Hartman, a pupil of Cannon's, stressed the idea that the adrenal cortical hormones exert a widespread effect at the cellular level in contrast to the more narrowly conceived

hypotheses of an "electrolyte-regulating" or a "prepotent carbohydrate-regulating function" (8).

II. Chemical Nature

1. Adrenal cortical steroids

To date, approximately twenty-eight steroid substances have been isolated from adrenal cortical tissue (9). However, only six have been shown to possess important biological activity, namely 11-desoxycorticosterone, 11-dehydrocorticosterone (compound A), corticosterone (compound B), 17-hydroxy-11-dehydrocorticosterone or cortisone (compound E), 17-hydroxycorticosterone (compound F) and 17-hydroxy-11-desoxycorticosterone (compound S). The evidence at present suggests that in man the adrenal cortex secretes preponderantly a single steroid, probably 17-hydroxycorticosterone (compound F) (10). However, it appears unlikely that compound F is the sole hormone secreted by the adrenal cortex under normal circumstances since the quantity of this steroid required for regulation of sodium and chloride balance would prove grossly excessive in respect to other functions mediated by this hormone. It is likely that an appreciable quantity of corticosterone (compound B) is also secreted normally by the adrenal cortex (11). The secretion of a combination of compounds similar to F and B could satisfy most of the known metabolic requirements of the organism. This does not exclude, however, the possible production of small amounts of desoxycorticosterone-like hormones which would exert a marked influence on sodium retention because of their great potency in this regard.

Whether or not androgenic substances similar to adrenosterone are secreted directly by the adrenal cortex or are derived entirely from degradation products of the 11- and 11,17-oxysteroids has not been established with certainty (12). The total androgenic effect of adrenal steroids is, generally speaking, thought to be derived from two sources: (a) degradation or intermediary substances arising from the 11,17-oxysteroids and (b) androgenic steroids secreted as such by the adrenal cortex. Some evidence for the secretion of androgenic steroids by the adrenal cortex under normal circumstances is suggested by recent studies which indicate that a dose of cortisone satisfactory for the maintenance of most bodily functions does not restore a normal level of 17-ketosteroid excretion in the urine of female patients with adrenal insufficiency.

At this point urinary products of adrenal origin should be mentioned. Only a small fraction of the compounds secreted by the adrenal glands are found as such in the urine. Urinary excretion of 11,17-oxysteroids and related compounds may be estimated as neutral reducing steroids, as formaldehydrogenic steroids, or as cortin biologically (13). The administration of ACTH induces a marked rise in the excretion of these types of compounds if an adequate adrenal cortical reserve is present. A majority of this increased steroid excretion consists of 17-hydroxycorticosterone or compound F (10).

The term "17-ketosteroids" is not synonymous with that of "androgens" although a variable proportion of urinary 17-ketosteroids exhibit androgenic activity (14). Some of these substances may originate as such from the adrenal cortex while 11,17-oxysteroids are also known to contribute to the 17-ketosteroids. Practically all of the 17-ketosteroids excreted in the urine of females are derived from adrenal cortical secretions; in the male approximately two thirds of the urinary 17-ketosteroids arise from adrenal hormones and one third from testicular androgens.

2. Adrenal medullary hormones

Since 1901, until very recently, epinephrine had been considered to be the sole hormone secreted by medullary tissue. However, with advances in the techniques of chemical identification it has been shown that adrenal medullary extracts contain at least two distinct compounds, with differences in physiological action: viz., "natural epinephrine" and "nor-

epinephrine" (15). The latter is distinguished chemically by the absence of the N-methyl group possessed by epinephrine. It is thought that under normal circumstances epinephrine constitutes approximately 80 per cent of the natural secretion of the adrenal medulla and nor-epinephrine probably less than 20 per cent. These data are derived principally, however, from animal extracts. Analyses of adrenal medullary tumors (pheochromocytomas) indicate that nor-epinephrine may represent as much as 90 per cent of the total hormone elaborated. The majority of cases of tumor in man in which analyses have been reported show values for nor-epinephrine in excess of 50 per cent (16).

Again, as in the case of the adrenal cortical secretions, it is possible that a series of closely related compounds may actually be responsible for the physiological effects previously ascribed to the single compound epinephrine, nor-epinephrine accounting for the vasopressor effects and epinephrine for central nervous excitation, glycogenolysis and cardiotonic effects. It is somewhat disturbing to realize that the solution epinephrine, standardized and accepted by the United States Pharmacopeia, actually consists of an unknown mixture of compounds which exhibit wide differences in physiological action. There is hope, however, that at last many of the conflicts and discrepancies which appear in the older literature in regard to the physiological action of epinephrine may be resolved by re-evaluating the action of pure epinephrine, nor-epinephrine and mixtures of these two compounds.

III. Physiological Action

1. Adrenal Cortical Steroids

A. 11-Desoxycorticosterone-like Steroids

The predominant effect of 11-desoxycorticosterone, when administered in physiological doses, is to retain sodium chloride and water and to facilitate the excretion of potassium (17). 11-Desoxycorticosterone modifies the electrolyte composition of the sweat and saliva as well as the urine. This compound is approximately fifty times as potent in its salt-retaining effect as steroids of the 11,17-oxy type (compound F). It has not been established conclusively that 11-desoxycorticosterone itself is secreted by the normal human adrenal.

The salt-retaining activity reflected by normal adrenal secretions and by adrenal extracts could be accounted for by the combined effect of compounds such as F and B (18), the sodium- and chloride-retaining activity of the latter compound being approximately one fifth that of 11-desoxycorticosterone and hence being intermediate between 11-desoxycorticosterone and the 11,17-oxygenated steroids.

B. Compound F-like Steroids or 17-Hydroxycorticosterone

There is good evidence to indicate that the human adrenal secretes preponderantly 17-hydroxycorticosterone or compound F. In man there is little, if any, significant-qualitative difference between the activity of compounds F and E (cortisone). The compound F-like adrenal steroids exhibit a wide variety of physiological effects in man which may be summarized briefly as follows:

a. *Regulation of Carbohydrate, Fat and Protein Metabolism*

Regulation of intermediary carbohydrate, fat and protein metabolism appears to be one of the chief functions of 11,17-oxysteroids (19). Glycogen depots are increased by (1) increased gluconeogenesis, (2) inhibition of glucose utilization and (3) increased utilization of fat. Compound F-like steroids increase protein breakdown and urinary nitrogen excretion. However, this effect may be modified by the adequacy of total caloric or protein intake as well as the initial state of nutrition. Increased uric acid excretion observed during the initial administration of cortisone therapy may be accounted for by a reduction in threshhold as well as an increased rate of uric acid formation.

b. *Electrolyte Regulation*

The electrolyte-regulating effect of the 11,17-oxysteroids is much less prominent than

that of the 11-desoxycorticosterone or the 11-oxygenated compounds (A and B) (20). Sodium and chloride retention is small unless massive doses of the hormone are administered. A transitory increase in urinary excretion of potassium is observed frequently. Its failure to occur may be explained by the deposition of available potassium in conjunction with that of glycogen. The long-continued administration of cortisone or compound F, in the absence of supplementary potassium medication, may lead to the characteristic picture of hypokalemia, hypochloremia and alkalosis.

c. *Androgen-like Activity*

Androgenic changes may be observed in patients given relatively large doses of compound F-like steroids. These are more marked in the female than in the male and are characterized by the development of acne, particularly on the forehead and face, and hirsutism. With excessive doses of these steroids, loss of scalp hair may occur.

d. *Regulatory Effect on Anterior Pituitary ACTH Secretion*

The continued administration of relatively large quantities of compound F-like adrenal steroids inhibits the pituitary secretion of ACTH with resultant atrophy of the adrenal cortex. It is not known whether this suppression is a direct action of the steroids on the pituitary alone or in conjunction with a physiological depression of the hypothalamic centers responsible for the regulation of anterior pituitary secretory activity.

e. *Effect on Thyroid Activity*

Compound F-like adrenal steroids or ACTH also have a depressing action on the uptake of radioactive iodine by the thyroid gland and, when used in large dosage, may result in a decrease in protein bound iodine (21). This inhibition of thyroid activity could be caused either by a decreased production of thyroid-stimulating hormone by the pituitary, a direct action on the thyroid itself, or on physicochemical changes decreasing the availability of inorganic iodine. This state may be reversed in part by the administration of thyroid-stimulating hormone from animal sources.

Cortical hormones of the Compound F type show a calorigenic effect not unlike that produced by thyroxin. It is of interest that in states of adrenal insufficiency thyroid hormone is less effective as a calorigenic agent than it is in normal subjects.

f. *Diuretic Activity*

There is evidence to indicate that following the administration of 11,17-oxysteroids there is a reduction in the serum and urinary values for antidiuretic activity (22). Such a change does not follow desoxycorticosterone therapy. Whether this change is brought about chiefly by an action of the 11,17-oxysteroids on the hypothalamus, posterior pituitary or liver is not known at present.

g. *Modification of Pigment Metabolism*

The administration of cortisone has resulted in a decrease in the pigmentation of some patients with Addison's disease. In contrast, large doses of ACTH administered to patients with intact adrenals have resulted in hyperpigmentation; the possibility of contamination of melanophore hormone has been considered a cause. Hyperpigmentation of the skin lesions in patients with dermatological conditions treated with cortisone has also been observed. It has been suggested that cortisone may inactivate sulfhydryl groups in the skin, thus permitting greater melanin deposition (23).

h. *Effect on the Neuromuscular System*

The neuromuscular changes which have been observed following the administration of compound F-like steroids are profound. Abnormalities in the electroencephalographic tracing which have persisted for years in patients with Addison's disease show remarkable improvement following adequate cortisone therapy (24). Euphoria almost universally appears during the early period of treatment with these steroids. Sleeplessness frequently accompanies excessive doses of cortisone or compound F

and frank psychoses may develop during the more prolonged administration of these hormones. Neuromuscular function is greatly improved in patients with adrenal cortical insufficiency treated with cortisone or compound F. When excessive doses of these steroids are given over prolonged periods, however, muscular weakness may develop in conjunction with chemical changes characterized by hypokalemia, hypochloremia and alkalosis (25).

i. *Hematopoietic Effect*

Compound F-like steroids are known to induce a reticulocytosis and polycythemia as well as to increase the number of circulating polymorphonuclear leukocytes (26). The administration of these steroids reduces the number of circulating eosinophils and lymphocytes (27). No consistent changes in platelets have been recorded in conjunction with the administration of cortisone or ACTH in normal states.

TABLE I

In Vitro Effect of Cortisone on Enzyme Activity

	KIDNEY	LIVER
Arginase	+	+
D-amino acid oxidase	−	+
Proline oxidase	+	−

j. *Anti-inflammatory Action*

These steroids appear to increase phagocytosis and, in culture, cortisone has been shown to increase the growth of macrophages in the spleen and lymph nodes (28). Fibroblastic proliferation, on the other hand, is impaired by these steroids (29).

Although much experimental work has been carried out in this field, it has not been shown conclusively in man that the administration of 11,17-oxysteroids inhibits or augments antibody production. In contrast, it has been shown repeatedly that the reaction of the somatic cell to the antigen-antibody complex may be diminished or in some cases abolished by appropriate treatment with these steroids (30).

It appears that the 11,17-oxysteroids tend to decrease the histamine content of tissue. This may be accomplished by a diversion of histamine precursors, as well as by an increase in histaminase activity (31). There is no evidence to show that the 11,17-oxysteroids block the local action of histamine injected as such.

k. *Modification of the Activity of Specific Enzyme Systems*

It has been demonstrated that the administration of 11,17-oxysteroids increases the secretion of gastric pepsin and the excretion of uropepsin (32). Serum peptidase activity is increased in man by ACTH and cortisone (33). High circulating levels of these particular hormones are also known to inhibit the activity of hyaluronidase (34). Cortisone is known to increase the activity of both kidney and liver arginase in contrast to testosterone which increases kidney arginase activity but not that in liver tissue (35). Experimentally, it has been shown that the 11,17-oxysteroids affect the concentration of liver d-amino acid oxidase without modifying the kidney concentration of this enzyme. On the other hand, the activity of kidney proline oxidase is controlled by cortisone, whereas the liver enzyme is independent of adrenalectomy and cortisone treatment (36) (Table I). The tissues of adrenalectomized animals appear to have an increased requirement for adenylic acid and ATP (36). This disturbance can be restored to normal by cortisone treatment. It has also been suggested that the 11,17-oxysteroids inhibit the rate of the peptokinase reaction.

C. Androgenic Adrenal Steroids

It is thought that steroids such as adrenosterone which have been isolated from adrenocortical extracts exert an androgen-like action, enhancing the anabolic functions of the body. Such an action would tend to oppose the catabolic effect of the compound F-like steroids. To date, however, no conclusive experiments have been carried out on man

with substances of this type derived from the adrenal gland.

2. ADRENAL MEDULLARY HORMONES

A. Epinephrine

The pressor and vaso-constrictor properties of epinephrine are well known and its effects upon circulation, respiration, skin, digestive tract and salivary excretion have been studied extensively. The outstanding effects of epinephrine upon metabolism consist of an immediate increase in blood sugar, blood lactic acid and in basal metabolic rate. The elevation in blood sugar is due to an increased rate of glycogenolysis in the liver; whereas the increase in lactic acid follows an increased breakdown of muscle glycogen. In addition, it is probably true that epinephrine has a stimulating effect on the hypothalamic-pituitary-adrenal cortical system in man (37) (Table II). Epinephrine has also been shown to exert an eosinopenic effect in completely bilaterally adrenalectomized man, which indicates an action on these cells independent of adrenal cortical hormone secretion (24).

B. Nor-epinephrine

The principal effect of nor-epinephrine appears to be that of constricting small blood vessels and consequently increasing blood pressure. Nor-epinephrine is relatively weak in its capacity to induce hyperglycemia or to stimulate the hypothalamic-pituitary-adrenal system (38).

3. INTEGRATED ACTIONS OF ADRENAL MEDULLARY AND CORTICAL HORMONES

A large series of carefully constructed experiments by Long (39), Harris (40), and Hume (41) indicates that epinephrine may act as a potent stimulator of the hypothalamic-pituitary-adrenal system. It is not known for certain whether epinephrine exerts its maximum effect on the hypothalamus or on the anterior pituitary directly, but it is evident that in the intact individual or animal the injection of a physiological quantity of epinephrine is sufficient to activate this mechanism. This knowledge leads one to postulate an integrated group of reactions under conditions of stress:

The liberation of epinephrine results in a rapid mobilization of blood glucose from preformed carbohydrate reserves and a rise in blood pressure due to a rise in cardiac output, while nor-epinephrine induces hypertension by an increase in peripheral resistance. In addition, the liberation of epinephrine initiates the stimulation of the hypothalamic-pituitary-adrenal cortical system. The increased secretion of adrenal cortical steroids permits the increased formation and hence replenishment of carbohydrate from non-carbohydrate sources, assists in the preservation of carbohydrate stores by decreasing glucose utilization and increasing the utilization of fat, and maintains blood pressure by maintaining blood volume through decreasing sodium chloride and water loss. Thus, the immediate stress is met by physiological mechanisms set in action by epinephrine, whereas the continued adaptation to stress is facilitated by those metabolic processes regulated by the adrenal cortical steroids. It is obvious that any impairment in medullary or cortical function must limit the adaptive capacity of the organism. It must be equally apparent that complete corticoid replacement alone following adrenalectomy cannot restore the natural response to stress in the absence of adrenal medullary tissue.

TABLE II

A COMPARISON BETWEEN THE PHYSIOLOGICAL ACTIONS OF EPINEPHRINE AND NOR-EPINEPHRINE

	EPINEPHRINE	NOR-EPINEPHRINE
Hyperglycemia	+	±
Tachycardia	+	±
Cardiac output	+	±
Peripheral resistance	−	+
Pituitary-adrenal activation	+	±

It should not be inferred from this discussion that epinephrine is the sole mechanism by which the adrenal cortex may be activated

(42). This appears not to be true since visual and other nervous stimuli, as well as changes in general metabolism which may not necessarily increase the secretion of epinephrine appear capable of increasing the activity of the pituitary-adrenal system. However, the fact remains that within the adrenals themselves there is the potential capacity for a coordinated response to stress characterized by immediate metabolic effects resulting from the direct action of epinephrine and more prolonged metabolic effects resulting from the activation of the pituitary-adrenal cortical system.

IV. Hypothalamic-Pituitary-Adrenal Relationships

Both the anterior and posterior pituitary secretions may be activated by stimuli of a wide variety. The mechanism by which the stimulation of centers in the hypothalamus induces increased liberation and synthesis of the trophic hormones of the anterior pituitary is a fascinating problem. The primordial nature of the cells in the hypothalamic centers, and the presence of secretory granules, along with venous communicating channels in which the direction of flow appears to be from the hypothalamus toward the pituitary gland suggest that the hypothalamus may actually secrete a chemical substance which under normal circumstances is carried directly by these vascular channels to the anterior pituitary (41). Obviously, if these substances gain access to the blood stream, the systemic circulation could serve as the vehicle for their transmission to the anterior pituitary. At all events, it appears likely that the sequence is: stimulation of the hypothalamus, the subsequent liberation of a chemical agent, the stimulation by this agent of the anterior pituitary with a resulting increase in the release of trophic hormones by this gland and the subsequent increased secretory activity of the cells of the target glands (thyroid, adrenals, gonads). Finally, a high titre of circulating target cell hormone exerts a depressing effect on further stimulation and secretion of the anterior pituitary gland (43). Again, whether the depression attendant upon a high circulating level of adrenal corticoids is mediated by a depression of the activity of the cells in the hypothalamic centers or a direct action on the cells of the pituitary gland, or on both, has not been conclusively established. The integrated action and the nice adjustment which such a "feedback" system provides for the regulation of metabolic activity is readily apparent.

In most physiological and clinical discussions the potential capacity of psychological stimuli for initiating and continuing the activity of the hypothalamic-pituitary-adrenal cortical system has not been fully appreciated. The susceptibility of these centers to psychic stimuli, with resultant chemical and physiological changes, could provide one explanation for the widespread effect which psychological and emotional factors often appear to exert on the systemic manifestations of disease. A knowledge of the fact that the pituitary-adrenal system may be activated as readily by psychological stimuli as by exposure to heat, cold, physical training or disease has many applications in the practice of medicine, both in its therapeutic implications as well as in providing a possible physiological explanation for some of the subtle cyclical variations often observed in the course of disease.

V. Response to Stress

An interesting study which illustrates the activation of the hypothalamic-pituitary-adrenal system in response to stress was carried out by this laboratory in conjunction with the annual Harvard-Yale crew race in 1950 (44). The extent of the reduction in circulating eosinophils was employed as a reflection of adrenal activation in the members of the crew participating in the inter-collegiate race. It was observed in these studies that strenuous physical exercise, i.e. a four-mile boat race, produced a profound fall in eosinophils, presumably the result of intense adrenal medul

lary and cortical activation. However, it quickly became apparent that in these well-trained individuals there was a better correlation with the degree of emotional and psychological stimulation than with the actual physical work involved. Thus, although equally good time was made by the crew in several practice sessions, the eosinophil fall was not as great in these tests as in the first practice race against time or in the final inter-collegiate race. Furthermore, the coxswain and coach, who exerted relatively "few foot pounds of work," exhibited a fall in eosinophils as great as in any of the crew! Emotional stress of itself or in combination with intense physical activity represented a maximal stimulus for the stress mechanism study; whereas this did not appear to be true of muscular activity alone. These studies suggest that stimulation of the adrenal cortex does occur with competitive strenuous exercise and that at least two major factors are involved: (1) intense muscular activity and (2) psychological and emotional stress. The evidence presented would therefore tend to establish more securely the importance of the cerebral cortex in the existing schemata of the stress reaction.

A practical application suggests itself: in unselected groups eosinophil counts made under conditions of standardized stress may well facilitate the identification of persons with unsatisfactory adrenal response to stress. The simplicity of the procedure would permit its use as a screening device. This study is also interesting in that it suggests in part an explanation for the very important role which a coach may play in the psychological and emotional preparation of a team for competitive sports. A thorough knowledge of the individual's reaction would facilitate the use of optimal preparation prior to competition. Obviously it is as undesirable to have an athlete below maximum reactivity at the beginning of a contest as it is to have a maximum stress applied so long beforehand that performance is limited by the early onset of fatigue or exhaustion.

VI. The Clinical Use of ACTH and Cortisone

1. as diagnostic agents

A. ACTH

One of the principal uses of pituitary ACTH at present is its specific action as an adrenal cortical stimulator and hence its value in estimating the reserve capacity of the gland (45). It is important in such application of the hormone to be certain that the hormone (ACTH) reaches the adrenal cortex; its failure to do so invalidates the information obtained. Because certain individuals who have received pituitary preparations in the past may destroy ACTH at an excessive rate locally on subsequent subcutaneous or intramuscular administration, it is important to check a negative response obtained under these circumstances with ACTH administered intravenously (46). It is also obvious that an indirect indicator such as the level of circulating eosinophils, while very convenient, should be used only as a screening device. Definitive measurement of adrenal cortical reserve will require the measurement of the blood or urinary level of adrenal steroids or their degradation products.

a. *The 4-Hour ACTH Test*

This represents a screening technique in which the activation of the adrenal cortex is measured indirectly by following the fall in circulating eosinophils (47). Patients with intact adrenals capable of responding normally will show a fall of approximately 70 per cent in circulating eosinophils 4 hours following the intramuscular injection of 25 international units of a standard preparation of ACTH.

b. *The 48-Hour ACTH Test*

The injection of ACTH intramuscularly over a 48-hour period with measurement in the change of eosinophils, 17-ketosteroid, and in selected cases of 11-oxysteroid, excretion has a much higher index of reliability than the 4-hour screening test (48). This is particularly true of hypoadrenocorticism secondary to pituitary deficiency. Recently, however, the

intramuscular or subcutaneous method of administering ACTH has been superseded by the intravenous administration of this substance because of the number of individuals who show resistance to hormones administered intramuscularly on successive occasions (49).

c. *The 8-Hour Intravenous ACTH Test*

A satisfactory and definitive test of adrenal cortical reserve consists in the injection of 20 I.U. of ACTH intravenously in 500 cc. of glucose or saline solution over a period of 8 hours. This may be repeated on several consecutive days. The change in 17-ketosteroids, and in selected cases of 11-oxysteroids, in the urine is measured, as well as the fall in circulating eosinophils, normally 90 per cent or more ten hours after the start of the infusion. A poor response, i.e. no rise in urinary steroids and a fall in eosinophils of less than 50 per cent, indicates adrenal cortical insufficiency or a poor reserve capacity; it does not distinguish between permanent or temporary exhaustion. A poor response initially, followed by increasing activation of the gland, suggests deficiency of ACTH, i.e. hypopituitarism.

B. Cortisone

Cortisone is of little diagnostic use in the detection of Addison's disease because of the difficulty encountered in evaluating the euphoria which so frequently follows the administration of this substance to patients with intact adrenals as well as to patients with adrenal cortical deficiency. Cortisone and ACTH, when given for any period of time, may be useful in detecting latent diabetes (50). Persistent elevation of blood sugar with glycosuria and ketonuria may suggest the presence of this metabolic defect years before clinical evidence otherwise would indicate the disease.

C. Epinephrine

A failure to show a 50 per cent or better fall in circulating eosinophils 4 hours following 0.3 mg. of epinephrine administered subcutaneously suggests anterior pituitary ACTH deficiency or primary adrenal insufficiency (37). In contrast, a fall in circulating eosinophils following epinephrine cannot be used as conclusive evidence of a normal pituitary-adrenal system since patients in whom both adrenals have been removed completely in recent studies in my laboratory have shown an eosinopenia of considerable magnitude following the test dose of epinephrine (51). Epinephrine has also been used in conjunction with radio-iodine uptake studies to demonstrate the potential capacity of the pituitary to release thyrotrophic hormone (52).

Epinephrine is of limited diagnostic value in estimating liver glycogen reserves. In this test the magnitude of the rise in blood glucose following the administration of a standard dose of epinephrine is measured.

2. AS THERAPEUTIC AGENTS

A. Specific Physiological Indications

a. *Substitution Therapy*

ACTH. Physiologically ACTH therapy is indicated in those patients who present signs and symptoms of adrenal cortical insufficiency secondary to pituitary deficiency. Because of the inconvenience of administering ACTH parenterally, and because of the tendency to develop resistance to certain hormone preparations with long-continued ACTH administration, its use in this group of patients has been reserved for the short-term administration of intensive doses of hormone in preparation for surgical operations which might be carried out on patients with pituitary deficiency (45). ACTH has been used to great advantage in the preparation of patients with brain tumors encroaching upon the pituitary and giving rise to symptoms of adrenal cortical insufficiency. When the hormone is employed in this manner, it is essential to allow 5–7 days for maximal stimulation of the adrenals. An effective means of stimulating the adrenal under these circumstances consists in the daily administration of 20 mg. of ACTH over an 8-hour period intravenously, the hormone being given in a 500 cc. solution of glucose or

saline. It is equally important to obtain demonstrable evidence of activation of the adrenal cortex, i.e. increased urinary excretion of 17-ketosteroids, 11-oxysteroids or a profound fall in circulating eosinophils.

A second use of ACTH which has more widespread application consists in using ACTH as a stimulator of the adrenal cortex to overcome the atrophy attendant upon long-continued cortisone therapy (53). Under these circumstances, it may prove feasible during the last two or three days of cortisone therapy to activate the adrenal cortex so that the period of adrenal insufficiency which ordinarily follows the discontinuance of cortisone therapy may be less severe and less prolonged. Again, the most effective means of stimulating the adrenal consists in the administration of 20 I.U. of ACTH intravenously over an 8-hour period (*vide supra*) (49).

Cortisone. The specific indications for cortisone therapy are (1) the treatment of Addison's disease, (2) the relief of temporary adrenal insufficiency associated with stress, and (3) the treatment of panhypopituitarism.

It has been observed that 25 mg. of cortisone given as a half tablet twice daily, in conjunction with 2 mg. or less of desoxycorticosterone acetate, provides, under normal circumstances, adequate maintenance therapy for most patients with Addison's disease (45). Occasionally patients will tolerate only 12.5 mg. of cortisone acetate daily because of excessive mental stimulation, sleeplessness and, rarely, psychoses on higher dosage. Twenty-five mg. of cortisone daily usually results in the correction of the abnormalities in the electroencephalographic tracing, diminishes the excessive anti-diuretic activity of blood and urine and ameliorates the disturbance in carbohydrate metabolism. During periods of stress caused by infection or trauma it will be necessary, of course, to increase the dose of cortisone to 100 or even 200 mg. per day.

Cortisone administered by mouth is absorbed almost immediately and the effect of a single dose tends to wear off in six to eight hours following ingestion. A single injection of cortisone intramuscularly exerts a more persistent effect, i.e. 24–48 hours. Thus, cortisone by injection need be given only once daily. With larger quantities of hormone, 100 mg. or over per day, injected intramuscularly, one may expect a continued, but diminishing effect for several days after the hormone is discontinued, whereas in the case of orally administered cortisone one anticipates a sudden abrupt deficiency of hormone within a day after the last dose has been administered. The temporal relationship of the effectiveness of the dose administered by various routes must be taken into careful consideration in the management of patients with adrenal insufficiency (54).

Relative or temporary adrenal insufficiency may be detected by the use of the ACTH test. Under these circumstances and in the absence of evidence of classical Addison's disease, treatment with cortisone should be instituted immediately. There are many medical and surgical emergencies in which patients appear to be unable to mobilize an optimum quantity of adrenal cortical hormones. Under these circumstances, substitution therapy may be employed to great advantage (55). The type of emergency and the patient's needs will determine whether cortisone should or can be given by mouth for its immediate effect or whether it should be given by intramuscular injection for its more prolonged effect. It is probable that within the near future a preparation of cortisone for intravenous administration will be available generally. It is obvious that an immediate high level of circulating hormone is the object of therapy in patients presenting acute adrenal deficiency.

Since it is not practicable in most instances to carry patients with hypopituitarism for long periods of time on ACTH, substitution therapy with cortisone is employed (24). Under these circumstances the dose and method of administration corresponds closely to that described under "treatment of Addison's disease". It is essential, however, to recognize that other target glands may be deficient, and that the effect of cortisone in

patients with hypopituitarism will be limited by associated thyroid deficiency. Conversely, the administration of thyroid alone under these conditions may be relatively ineffective unless cortisone therapy is administered simultaneously.

Adrenal Medullary Hormones. Since the syndrome of adrenal medullary hormone deficiency has not been definitely characterized, substitution therapy need not be discussed.

b. *Inhibition of the Adrenal Cortex*

Studies of Wilkins and others have now demonstrated conclusively that it is possible in patients with adrenal virilism to inhibit the secretory activity of the adrenal cortex by the administration of relatively small quantities of cortisone, i.e. 25–50 mg. daily (56). Reports to date indicate therapeutic success in patients whose adrenal cortices do involute under these circumstances. In these instances cortisone therapy must be administered for prolonged periods of time. Obviously the minimal effective dose of cortisone is the goal since cortisone itself in large quantities may give rise to an appreciable quantity of androgenic material among its degradation products.

c. *Physiological Antagonism*

An important clinical use of cortisone and ACTH is to employ the actions of adrenal secretions as antagonists to various physiological and clinical states. Thus, patients with hypoglycemia arising from a variety of causes might be helped by the administration of cortisone if specific methods of dealing with the problem are not available. Patients exhibiting a marked excess of anti-diuretic substance might be benefited by the "anti-antidiuretic" activity of cortisone. The bone-marrow stimulating effect of cortisone may be used to stimulate the activity of hypoplastic marrow under conditions in which the disordered marrow is not exhibiting a maximum response. There is no doubt but that as the physiological actions of cortisone and ACTH are better understood, the use of cortisone and ACTH as effective physiological antagonists will be extended (57).

The clinical uses of solutions of epinephrine and nor-epinephrine will not be discussed at this time since their indications are so well known and their application is familiar to all. The use of pure solutions of epinephrine and nor-epinephrine will permit the physician to use on the one hand an agent (epinephrine) which increases the blood sugar level rapidly, accelerates the heart action and stimulates the higher centers including the hypothalamic-pituitary-adrenal system; and on the other hand nor-epinephrine, the principal action of which is the pressor response effected by constriction of the small blood vessels. Most biological preparations of so-called epinephrine or "adrenalin" available today contain an unknown mixture of these two substances and hence the ultimate effect of a given dose will depend upon the relative quantities of epinephrine to nor-epinephrine contained therein. A number of synthetic substances possessing some or all of the properties exhibited by epinephrine and nor-epinephrine are also available for clinical use.

B. Non-specific Pharmacological Uses

The use of ACTH and cortisone as non-specific pharmacological agents implies the administration of these materials in amounts ordinarily considered to be in excess of those normally secreted. Furthermore, no specific deficiency of either of these agents is assumed to exist. It is impossible at this time to evaluate conclusively the merits of adrenal hormone therapy in many of these disease processes. The situation is complicated by the multiplicity of physiological and pathological features entering into the overall manifestations of disease processes in man.

High levels of circulating 11,17-oxysteroids are known to reduce fever and inhibit many of the toxic manifestations of bacterial agents or their breakdown products. Fatigue is alleviated and a sense of well-being often follows the administration of ACTH or corti-

sone. This may be accompanied by an improved appetite and consequent gain in weight.

It is becoming clear from the large amount of clinical information now at hand that adrenal hormones of the 11,17-oxy type exert a protective action on the living cell and on the metabolic processes intrinsic to normal function, this protection obviously varying with the type and amount of the injurious agent involved. This protective effect increases to an optimum with increasing doses of hormone, after which sufficiently high levels of these steroids lead to undesirable changes characterized by the well-known pathological picture exhibited in Cushing's syndrome. In therapy, therefore, an attempt is made to obtain the maximum protective action with the minimum of undesirable side reactions. Unfortunately, in many diseases the margin is an extremely narrow one.

The non-specific pharmacological uses of ACTH and cortisone may be divided most conveniently into (a) the treatment of those diseases or disorders which require a relatively short period of hormone administration, i.e. 5–15 days, and which are in general associated with a relatively high rate of remission, and (b) those chronic diseases in which prolonged remission or cure is rare despite extended periods of treatment with ACTH or cortisone, but in which the administration of these agents results in sufficient relief of disability to permit rehabilitation of the individual.

It is apparent, therefore, that diseases which respond rapidly to treatment are the most likely to be controlled and that cures can be expected only in diseases due to the temporary presence or action of a noxious agent. In such circumstances, short-term protection against the agent will tend to prevent the long-term sequellae which would of necessity follow an otherwise unimpeded inflammatory reaction. Thus, rheumatic fever, in contrast to rheumatoid arthritis, exemplifies the type of disorder offering the greatest possibility for lasting therapeutic success. However, even in chronic exposure to injurious agents, partial control of the disease may be achieved by low-dose maintenance therapy although a cure cannot be expected.

The non-specific pharmacological actions obtained in the body with the use of relatively large quantities of ACTH or cortisone may be grouped for convenience under four headings: (1) an anti-inflammatory type of action, (2) an anti-allergic type of action, (3) a diuretic action, and (4) a "euphoristic" action. Today the spheres of greatest usefulness of ACTH and cortisone as non-specific therapeutic agents may be summarized as follows:

a. *Collagen Diseases*

The relief obtained by patients with rheumatoid arthritis and the rehabilitation associated with cortisone therapy are well known (58). The number of prolonged remissions or "cures" resulting from a single course of ACTH or cortisone, however, is small. The greatest usefulness of adrenal hormone therapy in rheumatoid arthritis appears to be in the treatment of those patients who obtain sufficient benefit from a moderate dose of hormone to permit a more prolonged period of treatment without the development of undesirable side reactions. Care in preventing complications of excessive hormone therapy by supplementary potassium chloride intake in conjunction with sodium restriction have done much to facilitate the usefulness of these agents.

ACTH and cortisone would appear to have a definite place in the treatment of recurrent attacks of acute rheumatic fever (59). Dramatic cessation of the manifestations of rheumatic fever have followed relatively short courses of hormone therapy in a significant proportion of cases. It is not possible at this time to evaluate the possible role of adrenal hormone therapy in the prevention of rheumatic cardiac complications. However, it would appear probable that the rapid defervescence and restoration of normal pulse rate following hormone therapy in conjunction with the known capacity of the hormones to

reduce inflammatory reaction should prove helpful in diminishing or limiting the extent of cardiac damage produced by a given attack of rheumatic fever.

Patients with lupus erythematosus disseminatus receive great temporary benefit from the prolonged use of ACTH or cortisone; however, the number of cures is small, prolonged maintenance therapy is essential, and the ultimate mortality is high (60).

b. *Metabolic Diseases*

Acute and chronic gouty arthritis. ACTH and cortisone are useful in the management of both acute and chronic gout (61). These agents are capable of inducing a remission of acute gouty manifestations and in addition it has been possible for patients who have become intolerant to colchicine to resume colchicine medication while on cortisone therapy. It would appear that the combined use of colchicine and cortisone provides effective therapy for recurrent gouty arthritis at a relatively lower dose range for both drugs. Prolonged relief of discomfort has been observed with the continued use of 50 mg. of cortisone daily and 0.6 mg. of colchicine t. i. d., the disorder having been brought under control with temporary administration of larger doses of hormone.

c. *Hypersensitivity Reactions*

Hypersensitivity phenomena, including status asthmaticus, intractable hay fever, drug sensitivities, urticaria and contact dermatitis all appear to be indications for the use of cortisone or ACTH (62). Encouraging reports of benefit obtained in patients suffering from exfoliative dermatitis have also been confirmed (63). Again in these disorders patients with an acute skin inflammatory reaction of relatively short duration and with a propensity for remission will of course be found to be more susceptible to the action of the hormones.

d. *Ophthalmological Disorders*

Ophthalmological conditions comprise one of the most important and successful uses for ACTH and cortisone (64). Adrenal hormone therapy has been employed in such diverse conditions as acute iritis, acute keratitis, acute uveitis, acute choroiditis and sympathetic ophthalmia. Most of these diseases respond satisfactorily to a relatively short course of intensive hormone therapy.

e. *Miscellaneous Disorders*

Among other disorders in which the adrenal hormones have proved useful one should list the nephrotic syndrome (65) in which ACTH has provided one of the most effective diuretic agents although there is no evidence to indicate that the progress of the underlying nephritis is significantly modified. Beneficial results have been obtained in the treatment of early ulcerative colitis and it would appear that ACTH and cortisone are worthy of trial in patients who have proven refractory to other methods of treatment (66). At present ACTH or cortisone offer the greatest opportunity for effective treatment of pemphigus, and dermatomyositis, in the acute stages, has responded well. Chronic pulmonary diseases of the type which ordinarily progress to irreversible pulmonary fibrosis, such as berylliosis and sarcoid, respond to treatment with marked, but temporary, improvement in respiratory function. In acquired hemolytic jaundice effective remissions may usually be obtained and an occasional case of myeloblastic multiple myeloma may be controlled with this therapy. Acute calcific tendonitis and bursitis have shown dramatic response to ACTH treatment.

At present the most effective means of bringing under control in a rapid manner the manifestations of disease are: the use of ACTH intravenously in doses of 20 to 40 I.U., given over a period of 8 hours in 500 cc. of glucose or saline, or orally administered cortisone in relatively large doses, that is 200 to 300 mg. per day. For long-continued hormone therapy cortisone administered orally is perhaps the most practical method of treatment.

3. CONTRAINDICATIONS AND COMPLICATIONS

It is imperative that the greatest caution and care be exercised in therapeutic use of ACTH and cortisone in the following dis-

orders: (1) tuberculosis and syphilis, latent or active; (2) congestive heart failure and hypertension; (3) diabetes mellitus; (4) chronic nephritis; (5) peptic ulcers and (6) in patients with psychopathic personalities. Acute infectious diseases constitute a contraindication unless the administration of these hormones is combined with effective antibiotic therapy and the risk of masking the natural course of the disease fully appreciated (69).

The complications which arise in the use of ACTH and cortisone as non-specific pharmacological agents are the consequence of the abnormally high levels of hormone which are required to produce the desired anti-inflammatory change. The undesirable side effects most likely to be observed under these circumstances are:

A. Excessive Sodium Chloride and Water Retention

This is more marked with the use of ACTH than with cortisone, and can be obviated by careful restriction of sodium chloride when cortisone is employed and by the restriction of sodium chloride and *water* when ACTH is used since small amounts of pitressin appear to contaminate even the purest preparations.

B. Potassium Depletion

Perhaps the most serious complication encountered in the majority of instances is the gradual depletion of body potassium over a prolonged period of treatment. The metabolic disturbance brought about by excessive potassium depletion is characterized by a low serum potassium, a low serum chloride value and a relatively high carbon dioxide combining capacity. Hypochloremia in the presence of mild alkalosis should certainly suggest the possibility of potassium deficiency. This chemical aberration should not be permitted to occur and in most instances is easily prevented by the administration of potassium chloride in doses of from 2 to 5 grams daily in conjunction with adrenal hormone therapy.

C. Hyperglycemia and Ketosis

The precipitation of diabetes or the aggravation of diabetes is one of the complications which must be watched for during cortisone and ACTH treatment. Knowledge of this complication and adequate insulin therapy permit one to continue adrenal hormone administration if it appears desirable to do so.

D. Inhibition of Mesenchymal Proliferation

Excessively high doses of cortisone or ACTH may impair fibroplasia and normal healing (29). Thus either short-term or low-dose therapy should be employed in major surgery.

E. Androgenic Manifestations

The extent to which the development of acne and hirsutism complicate the course of cortisone and ACTH therapy will vary with the quantity of hormone employed and the individual susceptibility of a patient. Women, of course, are much more vulnerable to these changes than men. In most instances reversal to normal is observed within a matter of weeks to months following the discontinuance of adrenal hormone therapy. However, there are records of patients in whom these stigmata have persisted for a prolonged period following the withdrawal of hormone therapy. Occasionally patients develop hyperpigmentation. In cases in which ACTH has been employed this has been attributed to melanophoric contamination of the ACTH preparations. One also observes hyperpigmentation at the site of previous skin lesions cleared by large doses of cortisone administered over a prolonged period (70). This is in contrast to the diminution in pigmentation observed in patients with Addison's disease treated with small doses of cortisone.

4. CORTISONE AND ACTH AS TOOLS FOR INVESTIGATING UNKNOWN DISEASE MECHANISMS

As a conclusion to the present discussion, it may be of interest to indicate one or two of the exciting frontiers of medicine in which ACTH and cortisone promise to provide important keys to difficult problems.

In light of the marked effect which cortisone has been shown to have in correcting the abnormalities in the electroencephalogram observed in patients with Addison's disease, it was early

appreciated that one of the most important influences of this hormone might be related to its effect on brain metabolism. This was further suggested by the large number of patients who experienced euphoria when given cortisone and by the occasional patient who developed psychotic manifestations. The capacity of ACTH or cortisone to alter an individual's mood in a relatively short time has given the clinical investigator a unique opportunity to study the mechanisms involved in personality disturbances. Although there is little hope that cortisone or ACTH will prove particularly useful as a therapeutic agent in the majority of patients with psychological and emotional difficulties, it is apparent that these hormones may prove of tremendous value in outlining important fields for investigation.

The advent of cortisone has also provided an opportunity to evaluate further the role of the adrenals in diseases such as hypertensive cardiovascular disease, and nephritis (71). In the field of cancer there appears to be a real opportunity to use cortisone as an investigative tool. This is particularly true of patients with prostatic cancer who demonstrate recurrence after bilateral orchidectomy. Under these circumstances there is increasing evidence that the adrenal androgens may be a source of stimulation. The removal of the adrenals or the inhibition of adrenal cortical secretion by appropriate doses of cortisone may be an approach to this clinical problem. It is now possible to carry out bilateral complete adrenalectomy on such patients (72). Under these circumstances the ratio of adrenal steroids (cortisone/desoxycorticosterone) employed as substitution therapy may be modified to create a therapeutically beneficial hormonal background.

The fact that infectious diseases, such as tuberculosis, appear to be disseminated under the influence of cortisone therapy may provide an important investigative tool for a study of the mechanism of defense against chronic infectious disease. It can easily be seen from these considerations that the use of adrenal cortical hormones in the near future will provide a very important means of obtaining new information on a wide variety of pathological disorders.

Conclusion

In the wave of "adrenal enthusiasm" which is sweeping the world today one must assume that multiple factors, in addition to the adrenal secretions, are involved in the reaction of the organism to noxious agents. Important as the adrenal secretions appear to be clinically as protective agents in such situations, their ultimate contribution to knowledge and health will undoubtedly be correlated much more closely with the opportunities which they have provided for exploring intimate biological processes in a wide variety of pathological conditions than with their usefulness in the correction of any specific disease process.

For the unusual opportunity of being able to present these observations to you, under these auspicious circumstances, I am deeply grateful.

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The Value of Health Centers to the Community*

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NO MAN of dreams could feel more honor or be more honored than to have those who follow him press his dreams toward conclusion.

What we do here today and annually in this memorial address is to carry forward the interests and hopes of our illustrious predecessor James Meschter Anders.

As concerned as he was with the care of the sick, and as kindly as he was in his ministrations toward them, it must be so that Dr. Anders could not help but feel at heart that he, his times and his profession were somewhere at fault that there was still so much preventable sickness about. He must have nourished a righteous indignation against the continued presence of so many diseases that he knew could be prevented.

There is confirmation in his writings and in his acts as recorded by the many who have written and spoken of him that Dr. Anders was well aware of the benefits of Public Health and that he himself contributed in no small way toward its more general acceptance and usefulness. His deed of establishing the Annual Health Education Trophy in competition between the Junior High Schools of Philadelphia and his origination of Public Health Day are evidence of this fact. His establishment of the Preventive Medicine and Public Health Committee of the College of Physicians and his first Chairmanship of this Committee afforded him a medium for direct action in this same field. It is for these reasons that the College of Physicians honors James M. Anders by recalling his memory and perpetuating his interests through an annual oration on some aspect of Preventive Medicine and Public Health.

Our proud inheritance and the entire foundation of our profession tell us that we are dedicated to the relief of human suffering. From the beginnings of recorded history there have been those in every stage of culture and degree of civilization who have themselves chosen or been set apart by others to practice the healing arts. They may have been the medicine men of jungle tribes, the priests of religious cults, or the physicians of our own early centuries, but they all in common dealt with the immediate needs of their fellow sufferers with what means they had at hand, whether herbs, oracles or primitive medicaments and surgical tools. Occasionally too, through expediency or demands they tried to ward off the evil causes of disease by potions, incantations and fetishes of many kinds; an embryonic admission that prevention had its usefulness in forwarding their standing and prestige.

At no time in history has this feeble but important concept been lost to sight. But never too, has it ever risen to the position of first place among the possible means of alleviating human suffering. Even today amid the most widespread use of preventive measures the world has ever seen, the majority of physicians praise the work of public health, give lip service to it and the great organizations engaged in its promotion, but do little about it themselves.

Money is collected, appropriated and spent by the millions of dollars to find the causes of some diseases with the hope they may somehow be removed from us: articles in the press, magazines and lay journals run to countless printed pages to frighten, cajole or educate our laymen in the control and prevention of these same diseases. There are courses in our grade schools, high schools, and colleges put

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there for the same ends. Governments are expending billions of dollars to eradicate the agents and remove known causes of disease from our environment.

Throughout the world there is an unprecedented and hitherto undreamed of attempt to prevent the scourges of mankind and to drive the memories of them into corners of the globe from which there can be no escape and where they will be eliminated from our experience forever. From the health authorities of our most insignificant communities to the great International World Health Organization the battle goes on and there is no one who can deny that it is strategic and likely to be decisive in many quarters.

The publicity given to all these endeavors through every channel of communication and information has aroused all who hear and see it to the consciousness of a great belief that much disease can be prevented; it has created a painful feeling, intelligent or emotional, that many diseases to which we may be subject have no longer any excuse for being among us, and must go. With this the most sceptical, most cautious and conservative must agree; they have already been with us too long and we can tolerate them no more.

Let us join the sceptics for a moment; those who admit that this may be so of the plague, yellow fever, diphtheria, scurvy, or even typhoid, ricketts, and tuberculosis, all of which we know how to prevent, but what can be done now against diabetes, hypertension, arteriosclerosis, cancer and the like? Our too hasty hopes aroused by the billions of dollars spent and miles of inches of press lines printed must be quickly qualified with a conditional "so far as we are able;" those diseases which we know how to prevent must be prevented at all costs, but others, like cancer and heart disease must wait on knowledge which may come quickly or all too slowly.

While it is true that progress must wait upon knowledge we can take issue with the sceptics and face them with the fact that although knowledge must wait upon application the knowledge that we already have in these matters has been too little applied.

There can be little question but that within our own profession too many have taken refuge in the general feeling that the application of our factual knowledge against the causes of many diseases and states of ill health has been too difficult to try. Against this defeatism we can still say that had we in the past twenty years devoted sufficient energy and enthusiasm to the prevention of many of our common disease states we would be seeing far less of them today. We can say this because we do know the causes of many of our common diseases, we do know where they are vulnerable to attack, but we have not yet learned or tried sufficiently hard to provide the means by which our people can have these benefits brought to them or shown them how they can contribute adequately to their own health welfare.

The logic of the situation rests on the premise that no disease is inevitable. In this natural world we embrace the belief that it is an orderly world operating under natural laws some few of which have been revealed. In the realm of health and disease we submit to the concept that all of our biologic relationships and physiologic processes are governed by irrevocable laws of nature. On this level and in our world frame of reference we accept the natural principle of cause and effect and have no doubt that health and disease alike are the results of natural causes. In medical parlance we express this by saying that health is the result of effective causes and every disease or state of ill health results from known or knowable causes; that these causes may not all now be known is not important but acts only as a limiting factor in our knowledge of cause and effect in those particular cases which we may wish to study.

On this basis we can rest assured that disease may occur when the circumstances of the case are such that adequately effective causes have operated in such a way as to bring about the undesirable effects known as disease.

It is furthermore certain that since circum-

stances vary so widely in time and place the results of their action must be equally uncertain. The very fact that all people everywhere do not develop cancer, ricketts, diabetes or tuberculosis is evidence of the truth of this premise. The inevitability of any disease appearing in any individual is therefore relative and what appears to be unavoidable is so only because the effective causes have operated in a manner to bring about particular results in particular cases.

If effective causes do through various combinations or alone disturb our physiologic mechanism in such a manner and degree as to produce ill health or disease it is equally true that if these causes do not so operate those particular effects will not be realized and no disease will result.

The fundamental principle underlying the application of preventive measures lies in the fact that by deliberate effort on our part the circumstances under which known causes of disease act can be opposed or interfered with in such a manner that the results of their action can be so altered or diverted that the otherwise logical effects do not appear; the cause has been obstructed and the disease prevented.

All Public Health and Preventive Medicine rests on this sure assumption. The conquest of all of the great plagues and the phenomenal reduction in incidence, morbidity and mortality of many of our now common diseases have resulted from the deliberate or accidental interference with the chain of cause and effect which brought them about. Dr. Anders must have been well aware of this when he turned his interests so deliberately and effectively to matters of individual hygiene and collective attack against diseases of the community through the channels of Public Health.

The most certain fact that faces the future of medicine is the knowledge that the causes of all diseases can be known. That they are not all yet known is the mainspring of every endeavor to unfold the still mysterious origins of many of them. Every drive for funds, every detection clinic set up, every investigation in the natural history of disease has this one purpose; to reveal more than is now known as to why disease develops and to afford an opportunity to set about deliberately to combat disease at the earliest possible moment in its origin and development where it is vulnerable to attack. Curative medicine steps in to break the chain at some point even after disease has developed; diagnostic clinics are set up to detect the earliest evidences of disease before they have progressed too far for effective treatment; preventive medicine exerts all its influence to obstruct the agents of disease before they have resulted in pathology; Public Health is the action of constituted authority in the latter field.

The practical problem facing us is the determination of the ways and means by which a realistic application of the principles of prevention can be brought to and made available to the individual. Definite and effective methods have been reached long ago in the broad field of Public Health but no attractive and useful machinery has been determined for the maintenance of health and prevention of disease in the individual in that large category of disease states unapproachable through the methodology of Public Health.

There is overwhelming evidence that a large part of the population would welcome an opportunity to submit themselves to some program designed to keep them well and avoid disease provided it did not involve excessive expenditure of time and money and carried some fair degree of assurance that it would pay off. There are records of many failures to provide this service but they have all failed because they oversold themselves. Knowledge of preventive possibilities has run far ahead of the machinery for putting them into practice. Periodic Health Examinations have caught the imagination of many because their principles are sound, but their use has fallen into disrepute because the sponsors of the idea have tried too much with too little. The latest effort in this direction, for which I predict a failure, is the application of the principle of multiphasic screening; a process by which a naive faith in laboratory findings alone would

claim to elicit the presence or threatened beginnings of the topmost causes of morbidity and mortality in specific age groups. Nothing can come of this but a widespread sense of false security in those so screened and an atrophy of the medical acumen of those engaged in its operation. It might pay off statistically for a mass population so examined but the individual cannot be expected to be interested in being a statistical probability without specific assurance.

A realization has been gaining ground that official public health activities have been too far removed from the people. So long as our public agencies had to deal almost exclusively with environmental sanitation their problem was relatively simple. Health codes and regulations backed by police powers made it easy to promulgate controls over water, milk, food supplies, refuse disposal and the spread of communicable diseases. The inauguration of mass vaccination brought this machinery directly to the individuals. But none of these activities possessed the personal relationships necessary to remove the stigma of official necessity and develop the warmth of personal service that must be the keystone of understanding and wholehearted acceptance.

When official health agencies increased their interest in the Health of the Public it became evident that this field had extended into hitherto untouched corners that had not previously been searched into or thought of as their primary responsibility. Not too long ago no department of public health had considered it its duty to be concerned with the preventive problems of such conditions as cancer, heart disease and glaucoma. Knowing the futility of entering a crusade against such diseases through direct service, Public Health evolved the concept of Health Education and began to pour out propaganda against them by every means available to the processes of mass education.

More lately and quite recently, national, state and local health agencies both official and voluntary have come boldly forward and established direct service in these fields and contributed vast sums of money for research and study in them.

In spite of these herculean efforts the man on the street has remained relatively untouched. While it is true that hundreds of thousands have been X-rayed for tuberculosis and benefited directly thereby and thousands have been found with cancer, or precancerous lesions through cancer detection clinics, millions of our population have experienced none of this but have had their imaginations and fears aroused by the flood of truths and half-truths poured on them through the lay-press and well-meant health leaflets on all manner of diseases. In his fear often and in his intelligence occasionally he has looked up from his reading or stopped listening long enough to ask almost despairingly where he can seek competent advice and service to help him save himself.

The nearest approach to this many-faceted problem and one which would have been dear to the heart of Dr. Anders is the development of the District Health Center. It is true that this idea began to grow during his life-time, but not in the area in which he practiced.

The Health Center arose primarily as an extension of the central public health authority into the strategic divisions of its political sphere where most of its activities could be carried out in direct contact with the people of these areas. It afforded an opportunity for the authority to get into far closer touch with the people and thereby gain in mutual understanding and cooperation with them. It is beyond the scope of this presentation to review the details and operation of Health Centers but rather to point up the potentialities and possibilities that lie in them of carrying out the principles of prevention as previously discussed in forwarding the Health Welfare of all living within the area covered by the Health Center.

A Health Center is more than a decentralized unit of the Department of Health; it is a new Sociologic Unit that to be effective must be the focus point of all matters bearing on the Health Welfare of the community. It is

everything the health legislators have done in the past for the population as a whole and what the community must do in the future for its own health salvation. It above all else must be looked upon as a community responsibility although primarily sponsored and supported by the constituted health authorities; otherwise it is none other than an extension of the long arm of the law, the probing of the cold fingers of authority, the voice of a ghost living across the city in official isolation but shouting at the people through local loud speakers.

As to its total function, a Health Center is primarily dedicated to the prevention of disease and the promotion of health for the greater happiness, enjoyment of life and effectiveness of those of the community which it serves. These matters cannot be secondary to any others; they must be approached in a positive way and not be by-products of other approaches more directly the responsibility of agencies devoted to the diagnosis and treatment of disease and the giving of direct medical and surgical care.

In any organized community there exists a practicing medical profession, general and special hospitals and clinics and public and voluntary agencies for the care of the sick and disabled. The Health Center is an institution complementing all of these by operating in a sphere of activity in which Health comes first and consideration of disease comes after. This point cannot be emphasized too heavily for otherwise the Health Center would not only be duplicating the efforts of the others but missing its main objective that the others through necessity and divergence of interest can hardly carry out. This is not to say that in certain localities under special conditions the two approaches cannot or should not exist side by side or under one roof for the sake of economy and pooling facilities, but that if this is done the preventive aspects of the Center's activities must retain a clean cut autonomy with equal standing with the others.

The positive approach to health can only be obtained by consistent and single-minded attention to the factors responsible for the maintenance of health and those agents of disease known to be operating on the individuals and the community as a whole. Any departure from this principle will dilute its usefulness and result in abandonment of its main purpose; it will eventuate in increasing preoccupation with disease and its cure which can best be left to others.

Even a hasty review of the known causes of disease will reveal the fact that a Health Center has a unique opportunity to combat them. It can, through intimate knowledge of its clientele expose the factors of faulty inheritance in the family groups that come to it. The problems of food supply, costs of food and poor habits of its preparation and use are wide open for study on the community basis as well as on the level of individual deficiencies and excesses of nutritional factors that lead to so much ill health and disease. Every community contains hazards due to the presence in the homes, factories, places of occupation and in the air itself of harmful cosmopolitan, industrial and personal poisons. The presence and extent of them can be known and effectively opposed by improvement of community hygiene and instruction of the individuals on the presence of dangerous chemicals in the kitchen and medical cupboards of their homes as well as on the abuse and misuse of potentially dangerous intoxicants such as alcohol, tobacco and habit-forming drugs. Against the physical agents of disease all-out efforts can be made toward the prevention of accidents at home, at work, and at play and to fortify the defenses of the individuals against poor body mechanics by consistent attention and instruction in the hygiene of good posture, good exercise and good use in all ways of the physical bodies with which they are endowed.

The wide category of parasitic and infectious agents is too obvious to require extensive consideration here. Against this great group of causative agents are recorded the greatest triumphs of preventive medicine. Continued study and greater application of our knowledge about the diseases due to bacteria, viruses and

other parasites will lead eventually to greater conquests over the communicable, infectious and parasitic diseases.

The individual, the family, the group and the community are each a welter of psychologic clashes. As there are conflicts within the individual make-up, so there are similar conflicts between all individuals associated together in the community whether this association be so small as two individuals or as large as the entire social complex. It can be truthfully said that society itself is an organism and can exhibit in the mass all of the characteristics of an emotional-intellectual body most commonly thought to apply to the individual alone. The fears, anxieties, prejudices, maladjustments and conflicts involved in this complex are but a few of the causes of disease embraced in the broad category of psychobiologic and biosocial factors. In the same wide sense, mental hygiene is the approach toward their prevention.

A Health Center must develop a methodology of sufficient scope and efficiency as to embrace appropriate procedures against every known agent of disease. In some instances it will do this through broad projects against whole categories of disease-producing factors; in others it will institute special agencies against particular, individual factors.

The first necessary knowledge on which its action will be based will be the recognition of effective causes of disease it will be called upon to combat. The first organization on which it will build, beyond that of administration, will be the division of responsibilities among its activities so that together there will be complete coverage of the sources and agents of disease. Many of these divisions already exist in conventional health agencies. Public Health Departments of communicable disease control, tuberculosis case-finding and case-work programs, venereal disease control, maternal and child health, and mental health, environmental sanitation and its subdivisions are all in the central governmental organizations; at the Health Center they are decentralized units of the Health Department working directly and immediately with the people. In the community also are various voluntary health agencies whose support and assistance are invaluable on specific aspects of the Health Center's activities; they should be utilized to the fullest possible extent.

As indicated thus far a Health Center is seen to be doing those obvious things expected of it by utilizing all tried and effective agencies and procedures of accepted usefulness in the many categories of health work. What is not so apparent is the wide gap still existing between the known effective preventive measures in the mass and the almost untried means available for defense against disease in the individual. Mass X-rays, screening services and detection clinics are only a move in that direction. To complete the coverage against all disease agents, a method must be evolved by which all individuals, preferably in family units can have their health status evaluated, corrective and curative measures applied where needed by other community medical care facilities (including the private practitioners) and the resultant health level maintained by continuous health supervision and guidance. Such a mechanism for Health Maintenance with continued and unrelenting emphasis on Health must be the nucleus of the Center's activity; all other activities apart from their specific responsibilities must correlate their efforts with those of Health Maintenance.

At the very center of the organization must come Health Education. Every division and subdivision must utilize every method, procedure and facility of Health Education in order to make firm and solidify its efforts by creating the maximum of understanding on the part of each client of the clinic and of the community as a whole in the purpose, aims and activities of the Center.

Let it not be forgotten that a Health Center is a community facility and to it should be drawn all educational, religious, social and individual interests of the community that are concerned with its health welfare. There is no reason why its facilities should not be used as

a meeting place of any groups that have an interest in it. In the future it might well come to be said that one measure of the usefulness of a Health Center will be the degree to which it has attracted these ancillary units to itself. By the same reasoning a Health Center that remains unidentified with its broad community interests will be a failure.

Many organizations operating in the field of health welfare have not been referred to by name in this brief review of its functions but any Health Center in the very process of its establishment will quickly become aware of them and should utilize them to their fullest extent.

A Health Center is a Center for Health: Let it not encroach on other community measures devoted to the cure and treatment of disease and the giving of direct medical service, nor through over-ambition attempt those things beyond its immediate responsibility—the prevention of disease and maintenance of health of the individuals and the community to which it is assigned.

The value of a Health Center to a community can hardly yet be measured for none so far has embraced all its possibilities. Were I to attempt to measure one now I would check off the effectiveness of each of its activities against the known causes of disease. By such an amount as it attained or fell short of such coverage I would say that it is fulfilling or failing to fulfil its responsibilities and thereby show the measure of its value.

I feel sure that were Dr. James M. Anders with us today he would enthusiastically support the widespread development of Health Centers here and elsewhere and be among the first to accept the dictum that prevention of disease is the logical end of medical service.

Memoir of H. C. Bazett (1885–1950)

By FRANCIS HEED ADLER

Dr. Henry Cuthbert Bazett died suddenly on July 12, 1950, on his way to England to attend a meeting of the Physiological Society at Oxford. His death has taken from the College an eminent physiologist, who had recently been honored by the American Physiological Society in his election to the office of President.

Dr. Bazett was born in 1885, the son of Dr. Henry Bazett, of Gravesend, England. He was educated at Dover College, Wadham College, Oxford, and St. Thomas's Hospital. While holding a demonstratorship in Physiology at St. Thomas's, he was awarded the Radcliffe Traveling Fellowship in 1912, by means of which he was enabled to spend a postgraduate year at Harvard University.

He came to the University of Pennsylvania as Professor of Physiology in 1922, from the Christopher Welsh lectureship of Clinical Physiology at Oxford, England. From that time his outstanding characteristic, which was a dominating generous enthusiasm, won him hosts of friends and admirers in this country in addition to those abroad. In the laboratory and in the lecture hall he transmitted an energetic and infectious enthusiasm to all who came in contact with him. When relating or listening to accounts of experiments which revealed scientific truths or suggested new ideas of physiology, he became like a small boy given a long wished for toy. Age did nothing to diminish this ebullition of enthusiasm or his scientific curiosity, and it made no difference whether he was talking with one of his peers or a first year medical student, his attitude was always the same. This enthusiasm only handicapped him with those who could not keep up with the rapid workings of his mind. Things were so clear to him that he sometimes left out the numerous steps by means of which he had arrived at a conclusion, and occasionally left some listeners lagging behind. His other outstanding characteristic was fearlessness, and a willingness to subject himself to discomfort, if not actual pain, in the search for physiological truths. He himself was always the first subject of an experiment, and he often performed operations upon himself which most of us would hesitate to submit to.

In 1940 he obtained a leave of absence from the University of Pennsylvania to take part in aviation medical research, then starting in Canada. At the death of Sir Frederick Banting, Dr. Bazett took over the leadership of the medical research at the University of Toronto, and for this contribution to the war effort he was made a Commander of the British Empire in 1946. When he was engaged in the investigations of the effect of "G" in dive bombers, he would visit the various R. C. A. F. stations and ask in the mess who was the best and most daring of stunt pilots. Then he would persuade this pilot to take him up to see how soon the pilot could make him black out. It is reported that his numerous friends in administrative posts became so alarmed that confidential orders were sent to the stations that he was not to fly in such stunts, as he was too valuable to lose in such a way.

His contributions to physiology were many and varied. His greatest interest was in temperature regulation and in control of the circulation. Since most of this work was carried on in human subjects, and the subject who was employed in most of the experiments was Dr. Bazett himself, it was suggested by one of his friends that he should publish a book with the title, "The Physiology of H. C. Bazett."

No one could have worked with him without gaining in moral fiber from his courage, devotion to his work, and intellectual honesty. He never spared himself, and was generous with his advice and time to all who asked for it.

Memoir of William Rufus Nicholson (1868–1951)

By PHILIP F. WILLIAMS

Dr. William Rufus Nicholson, a Fellow of the College since 1899, and for many years its secretary, died in Philadelphia on February 18, 1951.

Dr. Nicholson sprang from a colonial lineage and was the great, great grandson of the Honorable Edmund Quincy of Quincy, Massachusetts, whose daughter married John Hancock, a signer of the Declaration of Independence. He was the son of the Rt. Reverend William R. Nicholson and Catherine Stanley Parker Nicholson of Boston where he was born February 26, 1868. In 1904, he married Dr. Delia J. Bolles, a young lady interne whom he met on one of his early hospital services. Dr. Nicholson's father was a highly respected Bishop of the Reformed Episcopal Church, and preached in the church of this denomination nearby on Chestnut Street.

After graduation from the William Penn Charter School, Dr. Nicholson entered the college department of the University of Pennsylvania taking a premedical course and graduating in 1890. Dr. Nicholson received a degree of Ph.B. at graduation, but years later, when applying for a chiefship in a Philadelphia hospital he found that all staff members had to have the A.B. degree. Since his undergraduate credits led equally to the degree of A.B., a change was made at his request on the University records, and Dr. Nicholson became an A.B, officially. His election to the hospital in question followed quickly.

Three members of his class in biology became members of the University of Pennsylvania college faculty: J. P. Moore, John Harshberger and Philip Calvert. Dr. Nicholson graduated from the University in 1893, an illustrious class, if one so defines a class from the number of professorships in medical schools held by its members in later mature years. After graduation, Dr. Nicholson served first in the Children's Hospital as interne and then secured the Pennsylvania Hospital interneship for two years. After a year of travel and study abroad, Dr. Nicholson settled near 16th and Pine, and among the dozen or more of his class whose offices were within a few blocks of his were: Sailer, Edsall, Taylor, Le Paul, C. Y. White, Riesman, Jopson and Stevens. The friendships this group formed on the campus at Penn continued for decades, especially in the University Club.

Dr. Nicholson had decided on an obstetrical career while still a student and never faltered in his determination to pursue it. He, like many others, was stimulated in this direction by the brilliant teaching of Barton Cook Hirst, who was his lifelong and intimate friend. This determination was a characteristic of Dr. Nicholson's life. I think he must have heard his father preach more than once on Ecclesiastes—9, 10: "Whatsoever thy hand findeth to do, do it with thy might."

Appointments in obstetrical and gynecological services followed one after the other. Dr. Nicholson served under Charles B. Penrose in the gynecology department at the University Hospital and simultaneously was an instructor in obstetrics. In 1900, he began as assistant to John M. Baldy in the Gynecean Hospital. Many of the reminiscences he told me when I was with him during my years as his assistant were based on his experiences with those two men. When Dr. John G. Clark came from Baltimore to follow Penrose, Dr. Nicholson became his assistant at both the St. Agnes and University Hospitals, and was at this time demonstrator of Obstetric Surgery under Richard C. Norris in the Manikin course.

Chiefships then began to come his way. He served first at the Maternity Hospital in Philadelphia now combined with the Lying-In Hospital, as the Women's Clinic of the Pennsylvania Hospital. From 1910, for 21 years, he was chief in gynecology and obstetrics at

the Methodist Hospital. In 1912, he was obstetrician to the Presbyterian Hospital, and served until 1933 when he resigned to devote full time to the Graduate School. He was elected chief of gynecology at the Polyclinic Hospital upon the closing of the Gynecean Hospital. When the Graduate Hospital was formed at the end of the First World War by a merger of several institutions, he became chief in Gynecology. In 1924, he became Vice Dean for the division of Gynecology and Obstetrics, and held this position for 22 years when he was made Emeritus Professor of these subjects.

He regretted tremendously that his age enforced his retirement from the duties in that institution a few years ago. He was proud to have held a teaching connection with the University of Pennsylvania for practically half a century. He taught with continued energy. He planned not only his own courses with meticulous care, but arranged with his collaborators in other institutions where his students went for clinical teaching that they should be given clinical instruction of the highest degree.

Dr. Nicholson preferred to teach rather than to write. Among titles in his bibliography is his Nathan Lewis Hatfield lecture in 1921 before this institution, entitled "An Anachronism of the Twentieth Century—The Midwife"; his observations and conclusions regarding the practice of midwives in the Commonwealth of Pennsylvania, a practice in which he was a consultant to the health department for a quarter of a century. Dr. Nicholson became a Fellow of the American Gynecological Society in 1916 and its Vice-president in 1939. He was a Fellow of the College of Physicians since 1899 and its secretary for a number of years. After his retirement from the University, he continued his activities in private practice and in the lectures and conferences in the Graduate School.

He had a fine sense of humor, a positive personality, and although he may have had a pretty quick temper in his argumentative moments, after the storm was blown over, he certainly never cherished a grudge. He was a loyal friend, brusque and honest, a gentleman, an excellent surgeon and teacher. His years of service in the Medical School of the University and particularly the energy and devotion he gave to the Graduate Hospital and to the Graduate School of Medicine have created a definite niche for him.

Chinese Medicine*

By WILLIAM W. CADBURY, M.D.

Emeritus Professor of Medicine, Lingnan University, Canton, China

WHILE western medicine has come to be widely accepted, especially in the larger cities of China, it is still only available for a small proportion of the common people. The writer during forty years' residence in Canton has been able to make personal observations of Chinese medical practice and to converse with native practitioners.

Prevailing forms of treatment of disease may be considered under two headings—superstitious practices and beliefs and the art of medicine as practised by the Chinese doctor.

The superstitious ideas deal with charms and magic fostered to a large degree by the Taoist priests. In Canton were to be found temples dedicated to the Spirit of Medicine or healing. Ignorant people, especially women, believe that the deity presiding in these temples can and will restore health upon the performance of certain magic rites and the payment of a small fee, but there is a philosophy back of these superstitions. Both priests and physicians share in the ideas handed down through the milleniums.

In the beginning was *chaos* or absolute void. Then evolved the *Tao* or the *Way*. Hence appeared the material universe and this in turn was divided into two elements the "Yang" and the "Yin", or the two cosmic forces. This dual conception represents the positive and negative, sun and moon, light and dark, acid and base, heaven and earth. The "yang" and the "yin" are generally represented as a circle divided into two parts each of which is a comma-shaped object resembling a tadpole. One is white and the other black or one is green and the other red. The circle stands for the great absolute and the two objects enclosed also represent the sunny and shady side of a hill. Surrounding the "yang" and the "yin" are grouped lines: straight lines typifying the "yang" and broken lines typifying the "yin". The combination is known as a pantagram. This pantagram was first designed about 2900 B.C. and stands as an emblem of the perfect balancing of the forces of the Universe.

While the Universe is considered as a macrocosm, Man is considered as the corresponding Microcosm. So we read that as heaven has its orders of stars and earth its currents of water so man has his pulse. As earth has its water courses called lakes, springs and rivers so man has his courses in the pulse—the three "yang" and the three "yin".

The Taoist priests explain these forces of the universe by personifications in the form of evil spirits or devils and the people are kept in constant fear of these demons of the air which they believe are always bent on bringing disease or death. Hence the superstitious practices resorted to for deceiving or warding off evil spirits. The priests recite incantations, paper money is burned and the pantagram hung over the doorway of houses. Demons are especially fond of marring beautiful children and so the parents invent disgusting names for the offspring in the hope of misleading these tormentors. Boys are especially liable to injury at the spirits' hands. Hence a guest should never inquire into the sex of a newborn child and a boy is often dressed as a girl and called by a female name.

The Chinese physician is quite a different personality from the Taoist priest although magic and astrology are inextricably bound in with his theories of the human organism. In the Chinese pantheon there are three revered figures usually placed beside each other and worshipped in the temples. Fu Hsi was the

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founder and chief philosopher. Next to him was Shannung who is supposed to have lived 2800 to 2700 B.C. and made a classification of some hundreds of medicinal plants. He was also the father of agriculture. The third member of this Triad was Huangti the careful observer. This third figure is known as the Yellow Emperor. Recently the "Yellow Emperor's Classic of Internal Medicine" (Huangti nei ching su wai) has been translated by Ilza Veith. Dr. Henry E. Sigerist, formerly director of the Johns Hopkins Institute of the History of Medicine, has written an interesting foreword. It is perhaps the most important of early Chinese medical works. By the Chinese it is regarded as the most influential medical book in existence. The translation into English makes about 120,000 words.

The Yellow Emperor is supposed to have lived 2697 to 2597 B.C. but it is not likely that the book was composed earlier than 1000 B.C., yet recent studies of the Shang Dynasty (1766 to 1122 B.C.) have revealed records on oracle bones of that period. A more likely date for the work is B.C. 249. According to the author, sound diagnosis is emphasized, based on the pulse and other physical signs.

THE CHINESE DOCTOR

In Chinese history there are recorded two eminent surgeons, Pin Ch'iao (2nd century B.C.) who made use of anesthesia and is reported to have exchanged the hearts of two of his patients. The most famous surgeon was Hua T'o (about 190 A.D.) His works were all destroyed except the report of his operation for castration. He had proposed the trephining of the skull.

Castration was a routine operation performed on the Eunuchs of the Manchu Court according to Hua T'o's method. The operation was also performed as a penalty for adultery. With one sweep of a sharp knife the genital organs were completely removed on a level with the skin of the pubis. A metal plug was inserted in the urethral opening and a cloth wrung out of cold water was applied to the bleeding surface and firmly bound on. The patient was allowed to drink no water for three days when the dressing was removed, the plug withdrawn and the patient allowed to urinate.

The body was said to be divided into three regions known as the upper or head; the middle or chest; and the lower or abdomen including the lower extremities. There are eleven organs: the heart, liver, lungs, spleen, left kidney, large and small intestines, stomach, gall bladder, urinary bladder and right kidney. The larynx passes directly into the heart which is the organ of thought together with the spleen. The urine passes directly from the small intestine into the urinary bladder through the ileo-cecal valve.

There are said to be 365 bones in the body. Viscera are divided into two groups known as the six viscera in which the "yang" resides and the five in which the "yin" resides. Each organ has a canal whereby it communicates with the other organs of the body. The blood is said to return to its starting point once every half hour instead of once in 25 seconds.

Each organ is related to one of the elements: fire rules the heart; metal the lungs; earth the stomach; wood the liver and water the kidneys. There is also a relationship with the planets and color and taste to the organs of the body.

Auscultation and percussion were quite unknown to the ancient Chinese doctor. Entire reliance is placed on palpation of the pulse and the general facies of the patient in making the diagnosis. Taking the pulse is almost like a solemn rite. It may be palpated at eleven different points, but usually the physician is satisfied with feeling it at the right and left wrist. With the right hand he feels the left pulse and with the left hand the right. Three fingers are applied—the ring, middle and index. With each finger applied on each of the two wrists he determines the state of one or more organs. The doctor applies weak, strong and moderate pressure to determine whether the pulse be superficial, deep or moderate. This must be done under nine complete inspirations. There are 24 main varieties of pulse. Ten minutes are often spent in the feeling of the pulse. When a doctor is

called he is summoned not to "see" the patient but to "feel the pulse".

Diseases are classified as external and internal. The former are those apparent on the surface, such as all skin affections, tumors growing on the surface and of more recent years all surgical conditions are classed in this category. Internal diseases include all fevers, diseases of the heart, lungs, abdominal organs and especially pulmonary tuberculosis, called "internal wound."

Perhaps in no line does the native practitioner show his ignorance more than in the treatment of fractures. No attempt is made to reduce the parts. A special clay is placed in a wooden bowl. The heads of several chickens are cut off while incantations are repeated and the blood is allowed to flow on the clay in the bowl. Blood and clay are now mixed together and applied to the fractured extremity. Bandages are used to bind on thin strips of bamboo. When the last turn of the bandage is being wound on, the blood of another chicken is poured in.

Coming now to the real field of the Chinese doctor, we find that the number and variety of remedies recommended in the Chinese Materia Medica can only be compared to our own National Pharmacopeia. The great Materia Medica compiled in the Sixteenth Century is composed of 52 books and contains 1892 remedies. Among the most used drugs are some that are found in the western pharmacopeias, such as ginseng, rhubarb, sulphur, pomegranate root, aconite, opium, arsenic and mercury. A remedy that I have not infrequently seen applied to a patient in extremis is as follows: A rooster is killed and the body cut in half, longitudinally, and the bleeding half is quickly applied to the skin of the patient's abdomen. If there is any possibility of a cure this is supposed to be infallible.

The use of the acupuncture needle seems to be seldom resorted to in the neighborhood of Canton. The theory on which it is based is that if one punctures the blood vessels connecting different organs the disease will be aborted. Three hundred and eighty-eight points suitable for acupuncture are described. There is a manikin in use in Peking pierced with holes at all the suitable points. Paper is pasted over it and the student must locate the suitable point through the paper. Needles are from $1\frac{1}{2}$ to 28 cm. in length and are made of gold, silver or steel. During the operation the patient coughs and the errant humors are directed back into their normal courses.

Moxa or the use of the cautery is another of the traditional remedies much resorted to in some areas of China.

The present trend in official circles of the Chinese empire is to turn aside from all the innovations brought to China by western missionaries and other representatives from the United States and Great Britain. Modern medicine is the great exception to this rule. The medical schools and hospitals built up during more than 100 years after models introduced from the west are still functioning although there is a tendency to cut down the preliminary or premedical courses and shorten the years of medical education. Western Medicine is one of the contributions from the West which will be preserved.

Moorestown, New Jersey.

Plato and Psychosomatic Medicine*

By NICHOLAS PADIS, M.D.

"PHILOSOPHY begins in wonder," said Professor Whitehead, "and at the end when philosophic thought has done its best, the wonder remains."

And medical thoughts, like philosophic thoughts, begin in wonder too; and even if an answer is obtained, the wonder not only remains but expands to labyrinthian proportions.

In the beginning medical ideas were mystical and philosophic; then they became more philosophical than mystical; then religious, semi-scientific and philosophical; and at the dawn of the twentieth century, medicine became again skeptical on this eternal dualism of human existence, the relationship of body and soul.

In a sense, ideas are biological entities, subject to their forces of heredity and environment. The so-called revolutionary scientific ideas, if critically examined, are but mutations. In the history of medicine or that of mankind at large, there is greater evidence of the immortality of an idea, than that of a protoplasm.

An idea, as a living entity, is also subject to the same creative and degenerating forces of Time. Time, the supreme, universal creative force, adding and subtracting, multiplying and dividing, creating new worlds in the life of man, but out of the same matter that contains the same forces, probably now metamorphosed, or sublimated. And although modern biologists speak of Biological Time, Hippocrates, creator of our scientific medical world, concluded that "Chronos o protos Theos"—Time is the first God.

In the dark medical skies of 1935, a comet appeared and as such attracted much attention. It was brilliant; brilliant as never before, and a new name for an old comet was necessary. Such was the rise of psychosomatic medicine by the publication of *Emotions and Bodily Changes* by Dunbar; the efforts were a crystallization of the ideas of body-mind relationship that were revived in the beginning to this century. It was fortunate that Dunbar chose 1935, for two years later Medicine entered definitely into the era of chemotherapy and antibiotics; and in a few years dawned Selye's gospel of adaptation syndrome—discoveries that have contributed a great deal to the modern concepts of psychosomatism in the practice of medicine.

In surveying the rather neoplastic growth of psychosomatic medical literature of recent years, one is impressed with the fact that psychosomatic medical knowledge carries the same air of up-to-dateness as that of cortisone and ACTH. A very good example is the title of a chapter, "Twenty Years of Psychosomatic Medicine," in the recent *Twentieth Anniversary Review of the Josiah Macy, Jr. Foundation.*

But for historical accuracy, Dunbar's first paragraph in *Emotions and Bodily Changes* starts with the voice of Socrates, the spirit of Plato, the highest expression of Greek civilization; "Socrates reported to his Greek countrymen that in one respect the barbarian Thracians were in advance of civilization. They knew the body could not be cured without the mind. 'This,' he continued, 'is the reason why the cure of many diseases is unknown to the physicians of Hellas because they are ignorant of the whole.' "

The purpose of this presentation is not to introduce a psychosomatic atavism or to present, according to Plato, a form of misology; for he states, "But first let us take care that we avoid a danger . . . lest we become misologists. For as there are misanthropists, there are misologists (haters of ideas) and both spring from the same cause which is ignorance of the world." To the contrary, it is an effort to reflect some of the classical ideas on the dualism of body and soul, as conceived

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by Plato during the Golden Age of Greece. "It is to Greece, the mother of Europe," states Whitehead, "that we must look in order to find the origin of our modern ideas." And in this particular case, the Greeks not only had a word for it, but have offered some very fundamental principles about it.

The growth of any idea depends on its biological time. Plato's thoughts on the interrelation of body and soul were overlooked in Athens and in Rome, due to the prevailing Hippocratism at that time. It was a revolt against mysticism which was partly transmitted to Aristotle and to Galen as well. Yet it was this Greek medical trinity—the fatherhood of Hippocrates, the universal love of Plato, and the realism of Aristotle; and later the St. Paul-like psychosynthesis of Galen—that ruled medical thoughts for centuries.

The Hippocratic School emphasized observations on the body as a whole. Plato emphasized the constitution of the patient and states, "And I said of medicine, that this is an art which considers the constitution of the patient and has principles of action and reason in each case."

Plato's philosophy of medicine is conspicuously absent from present-day books of medical history. Again it was the medico-philosophic genius of Osler that brought to light and displayed the brilliancy of the Platonic medical thoughts. In his immortal *Aequanimitas*, there is an essay on "Physic and Physicians as Depicted by Plato," delivered in 1893 at the Johns Hopkins Hospital Historical Club. In his introduction Osler states, "From the Hippocratic writings alone we have a very imperfect knowledge of the state of medicine in the most brilliant period of Grecian history. . . . We are fortunate in having had preserved the writings of the two most famous of the Greek philosophers—the great idealist, Plato . . . and the great realist, Aristotle."

Osler speaks of Platonic medical ideas as crude and imperfect, as much or even more so than those of Hippocrates. But as to his psychology, he says, "The psychology of Plato, in contrast to his anatomy and physiology, has a strangely modern savour, and the threefold divisions of the mind into reason, spirit, and appetite, represents very much the mental types recognized by students of the present day."

Such modern psychological, rather psychoanalytical, concepts are revealed in *Timaeus* where Plato's ideas on Eros and the Soul are too Freudian or vice versa. Discussing the love of procreation in the human, he states, "The animal within them is desirous of procreating children, and when remaining unfruitful long beyond its proper time, gets discontented and angry, and wandering in every direction through the body, closes up the passages of the breath, and by obstructing respiration, drives them to extremity, causing all varieties of disease."

Through Eryximachus, the Physician, Plato says in the *Symposium*, "And from medicine I will begin that I may do honour to my art. There are in the human body two kinds of love which are different and unlike . . . and the desire of the healthy is one, and the desire of the diseased is the other."

Raphael Demos, in his classical analysis of the philosophy of Plato, says of this relationship of body and mind; "And, finally, the soul with the body finds itself in a relation with the general physical environment, and also with other human beings. We have thus four components: immortal soul, mortal soul, body, and the physical-social situation.

"The first two constitute the human soul; the last its environment; and the body functions as the go-between. Human life is an integration of these four motions. The good life in this world depends upon the harmonious co-operation of all four factors; a well-functioning reason requires a healthy body; . . . In a semi-humorous passage, Plato raises the question why the intestines of the body happen to be so long; and he answers it by saying that the creator was aware that the human race is intemperate in eating and drinking and liable to take in a good deal more than was necessary, by reason of gluttony. He therefore bestowed on us long intestines which have the

effect of protracting the period of digestion, of prolonging the interval between meals, and so of providing sufficient time for the discussion of philosophy (*Timaeus* 72d)."

And in *Timaeus* again, Plato expresses these thoughts with a definite modern psychosomatic tone: "So likewise we conceive of the compound of soul and body which we call 'living creature.' Whenever the soul within it, is stronger than the body and is in a very passionate state, it shakes up the whole body from within and fills it with maladies; and whenever the soul ardently pursues some study or investigation, it wastes the body; and again, when the soul enrages in public or private (and battles of words carried on with controversy and contention), it makes the body inflamed and shakes it to pieces, and then induces catarrhs; and thereby it deceived the majority of so-called physicians, and made them ascribe the malady, to the wrong cause."

Zilboorg, in his excellent book, *A History of Medical Psychology*, presents the Platonic ideas as mystical and idealistic and definitely deviating from the empirical attitude of Hippocrates. Probably this is true if one considers only the history of mental diseases. But one is aware of the revolutionary attitude of Plato towards the medical conceptions of the School of Cos when Socrates says to Charmides, who was complaining of a headache, "... and therefore if the head and the body are to be well, you must begin by curing the soul; that is the first thing. For the great error in our day in the treatment of the human body is that physicians separate the soul from the body."

It is because of such immortal Platonic statements that Professor Jowett, one of the great interpreters of Plato, says of him, "... more than two thousand and one hundred years have passed ... yet the echo of his words continues to be heard among men ... because he is always moving onward ... and knows that truth is greater than consistency."

Such is the inheritance of the present-day conception of this complex inter-relationship of body and mind—this new scientific discipline, according to Dunbar, known as psychosomatic medicine. But scientific discipline alone in present-day practice of medicine is inadequate. As man increases his span of life and thus unfolds the potentialities of his body and mind to an everchanging environment, scientific medical thoughts reveal their tragic limitations. Human life cannot be measured by science alone. Medicine is entering a new era, which the historians of the future may call psychosomatological determinism. Plato's ideas then that man is a composite creature and related to all the universal forces that surround him should be accepted.

But under such a concept, practice of medicine would be neither an art nor a science, but an idealism.

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Our Old Spectacles

By ELLA N. WADE

Curator of the Mütter Museum and Custodian of the College Collections, College of Physicians of Philadelphia

AMONG the interesting exhibits to be found in the Mütter Museum of the College of Physicians is a collection of old spectacles. Little information came with any of them. Invariably they were presented merely as "old spectacles", and in that way they have been catalogued and labelled.

Recently we received for the College Collections, a collection of spectacles from Dr. Burton Chance, numbering over sixty, many with their original cases, and the donor promised to come in sometime and help to identify them. But Dr. Chance is a busy man, so the curator thought the least she could do, after receiving such a splendid collection, would be to find out something about spectacles herself. Some material on their history was found in the College library, and Dr. Chance kindly supplied many interesting and informative pamphlets, so that now the major part of the collection may be identified and classified.

Although it is probable that the history of spectacles is well known to most, it was thought that a brief review of their invention might prove interesting to those who are not familiar with it, and might also stimulate interest in our own collection.

It is hard to picture a world today without spectacles—a device indispensable, but one that we take very much for granted. Progress in literature, art, science and industry is dependent on them, for the major part of our education is obtained by using our eyes. Unfortunately we are not all born with good ones, and there are few who are permitted to live out life's span without resorting to the use of eyeglasses sooner or later. In fact, without them many would be unable to earn a living after middle age.

Since printing, with movable type, was not invented until the early part of the fifteenth century, and the few books that were available were hand-written and costly, and because few men could read or write anyway, there was no special need for spectacles to aid those with poor or failing eyesight before that time. We are told that in Spain they first were used as an article of adornment, and to add dignity to the appearance of the wearer. After their introduction into Spain they soon came into general use, and a Spaniard, Benito Daça de Valdes, wrote the first scientific book on them in a modern language, in 1623.

In France, however, spectacles were worn to hide defects of the eyes. It was not fashionable to wear them in public, so lorgnettes were introduced, which could be used only when needed.

While it is unlikely that the present generation wear eyeglasses solely to adorn their person, as did the Spaniards, many who are obliged to wear them to aid the sight, also take into consideration their personal appearance, and we see women, thinking to make themselves more attractive, wearing oddly shaped spectacles with frames in colors to match their costume, some even ornamented with imitation jewels or heavy gold inlay. Opinions differ on the resulting effect.

In the 1600's the value of eyeglasses began to be recognized in many countries, and eyeglass peddlers did a profitable business going from house to house, allowing those who could afford them to choose the pair best suited to them. This practice continued for many years.

In these days poor eyesight as well as other unhealthy conditions are recognized in early childhood by the doctors and nurses supported by the public schools, and at once steps are taken to remedy them. How often we see a

tiny tot, looking like a wise little owl, peering through a pair of shiny spectacles, without which he might appear dull and stupid, not because he is mentally retarded, but because of his impaired vision. I am reminded of a small boy in my own teaching experience, who seemed bright enough when quizzed orally, but who was unbelievably stupid when confronted with work to be done from the blackboard. I finally discovered that he was so near-sighted that the problems, words and sentences on the board looked, as he expressed it, after much questioning, "like a lot of different kinds of white fences." He could distinguish no letters or figures from any seat in the classroom. There was no school doctor for this small rural school, and his parents, apparently, had never become aware of the defect, so he started his education with a decided handicap. Remedial glasses were obtained for him and we found him to be as bright as any pupil in the class.

After reading many articles on the history of spectacles, we learn that no one is quite sure who first invented them, although a Florentine, Salvino D'Armato, who died in 1317, is generally credited with their invention, and Alexandro de Spina with making the invention public. The two men, it is said, heard of the lenses first described by Roger Bacon, inventor of the telescope, in 1276, and conceived the idea of putting them in frames to aid those with poor or failing vision.

The first eyeglass was a single lens—a magnifying glass—set in a frame and attached to a handle, by which it was held to one eye. These appeared in the last half of the thirteenth century. As it was hard for some to see, using only one eye and keeping the other one closed, these handled monocles were doubled, and the "scissors-spectacles" developed. The two lenses were placed where the blades of the scissors would be, ordinarily, and when the handles were closed by the user, the lenses spread out before his eyes.

In the thirteenth century, when the single lens was used, it was called a "spectacle." Later when two of these lenses were joined together with a nail or pin to serve both eyes, they were called a "pair of spectacles." Because these "nail-spectacles," as they were called, would not stay on the nose, the wearer was obliged to hold them on by the bridge, where sometimes a small knob was placed for convenience. This type disappeared after 1500, when a round bridge replaced the awkward angle formed by the union of the two monocles.

While this improved type was much more comfortable on the nose than the angular "nail-spectacles," they still were no easier to keep on, so, as reading became more popular with the advent of printing, some method whereby they could be affixed firmly to the nose had to be found, and this was accomplished in many strange ways. One unusual way was for a spring to be attached to the bridge of the spectacles, and passed through the hair and under the headgear to the back of the head. Sometimes this was fastened to the hat. Still another method was for a metal band to be fitted around the head and supplied with small hooks at the forehead on which to hang the lenses. Strings attached to the sides of the spectacles and running over the ears, with small weights at the ends to keep them in place, were also tried.

Spectacles with bows did not appear until the middle of the eighteenth century, and they were called "temple-spectacles" since the flat metal side pieces reached only to the temples, the ends terminating in round flat rings or cushions that allowed them to press into the temples, with a minimum of discomfort, and so hold the glasses more tightly to the nose.

These temple bows were gradually lengthened by adding a second piece with a double jointed hinge which folded inward behind the head. Later this second temple was shortened and directed downward behind the ears, and from this developed the curved end fitted behind the ears that are in use today. It seems strange that such a long time should elapse before anyone discovered that the ears could be used for something besides hearing. They make a perfect anchor for spectacles.

Many of the old spectacles of our grand-

father's day had the slender metal side piece that curved inward slightly to press firmly enough against the head to hold them in place. Today, also, eyeglasses are constructed in this manner so that they may be slipped off and on quickly and easily.

As many of the people of the eighteenth and nineteenth centuries still preferred the arrangement where the bows met at the back of the head, the telescope spectacles were made. In these, the second flat side pieces were made so that they would slide back and forth along the first, and be reduced in length when the glasses were folded.

As the construction changed, so also did the materials of which the lenses and frames were made. Quartz, beryl or other semi-precious stones were used for lenses before the manufacture of transparent glass was perfected, so that people wearing spectacles were sometimes spoken of as wearing "beryls." Frames were variously made of leather, horn, wood, tortoise shell, iron, copper, gold and silver. From 1500 up to 1600 the frames were almost entirely made of leather, as it was thought leather did not slip so easily. The oldest known pair were found in Nürnberg in the house of Wilibald Perkheimer, a supporter of Martin Luther, when the house was being taken apart to be moved to Wartburg, Perkheimer's birthplace.

The first spectacles were rather cumbersome, having large circular lenses and heavy frames. Lighter frames with small oblong and oval shaped lenses followed, and in the late eighteenth and nineteenth centuries these had become very small indeed.

A few years ago rimless spectacles were in vogue and they are still very much in favor, but we also seem to be reverting to the large circular lenses and, if not heavy, at least heavy appearing frames of plastic or tortoise shell.

Naturally with the change in shape and size of spectacles the cases changed, and often, in a collection of old spectacles, the cases are as interesting as the glasses themselves.

We cannot boast of very many ancient spectacles, but still the Museum and College collections are interesting ones. The ancient Chinese glasses are the oldest—just how old we do not know. Although it is thought that the Chinese may have been using spectacles before they were known in Europe, there are no writings to substantiate the fact. One ancient Chinese pair in our collection has large circular lenses of dark glass. The hinged bows are attached to the outer edge of the lenses, and end in flat metal discs. The bridge is of the same heavy metal. Quite different is another pair also labelled "ancient Chinese." This frame is made from one piece of tortoise shell and the lenses are only about the size of a twenty-five cent piece. The short bows are attached to the elongated sides of the rims. Tortoise shell was used by the Chinese for frames because it was thought to be lucky, as the tortoise is sacred to the Chinese.

The Chinese often wore frames with no lenses, considering spectacles to be a badge of supreme social and educational standing. In fact, Dr. Chance said that the ones he presented to the College, and which were brought to him from China, while they have lenses, were not purchased to aid the sight of the owner, but to give him an intellectual appearance.

The old Japanese spectacles in our collection differ very little from those of the Chinese. The shape and construction of the cases are identical, although the one from Japan is elaborately embroidered in colored silk and decorated, at the bottom, with two red silk tassels, while the Chinese one is of plain black lacquer. In each instance, about one-third of the case forms the top, through the center of which a cord runs from the inside of the case. There is a knot in the cord about two inches above the top of the case, in the Chinese specimen, and a bead is placed in the same position on the cord in the Japanese case. This knot and bead allow the top to be removed only far enough to remove the spectacles—a novel way to insure against the loss or mislaying of part of the case. The spectacles, in their case could be, and probably were, carried by this cord.

The modern Chinese spectacles differ very little from the ancient ones in shape and size.

The lenses, like the ancient ones, are large and circular, but the frames are much lighter.

Two pairs of Chinese spectacles, recently given to the College by Dr. Chance, must ante-date those mentioned above, for they have no bows or nose pieces to hold them in place. The rims are of horn, and the arched bridge is very heavy with a hinge in the center, allowing one lens to fold over upon the other. Two holes are made in the horn on the outer side of each rim for attaching loops of string by which they were either tied behind the head or looped over the ears. Folding glasses are no new invention, but are a readaptation of these from ancient China.

We have no specimens of the ancient "nail-spectacles" although one in the recent collection from Dr. Chance is very similar. In this one, the short handles of the two monocles are joined by a pin, forming an angular bridge. Unlike the old spectacles, however, the right rim extends out into a ring whereby they may be held, or a cord or ribbon attached so they could be worn around the neck. They are really a type of folding spectacles used during the eighteenth and nineteenth centuries.

In our collection, aside from the many that are fairly modern, and in use during the last thirty or forty years, we have many of those with the jointed bows, both reaching behind the head and dropping behind the ears. There are many, also, with the small narrow lenses, varying in shape, in clear and green glass, with the telescope bows that were used during the late eighteenth and nineteenth centuries. Many of these have the extra side lenses which helped to shield the eyes from the light, among them being a pair of dark glasses worn by John Greenleaf Whittier to rest his eyes while travelling.

We have a variety of those spectacles known as "nose glasses"—some of them being the Oxford type. Many dating back about sixty years have a flexible bridge and pieces for the nose. The lenses are of medium size, oval and rimless.

One pair of nose glasses, recently received, was made in Poland, and are fitted to the nose in a unique manner. The straight bridge is rigid and made up of two parts. To one lens is attached a small straight rod of metal, set in a wire spring. To the other lens is attached a piece consisting of two parallel rods about a quarter of an inch apart. The one rod with the spring slides through this aperture, forming the bridge. The wearer must pull the two lenses apart, fit the nose pieces onto the nose and release the lenses. The spring allows the two lenses to come together again, pinching the spectacles firmly into place. It seems to be an excellent arrangement.

We regret that we have no spectacles used by Benjamin Franklin, who is credited with devising the first pair of bifocals. Dr. Joseph McFarland, a former curator, tried zealously to get a pair that he knew existed, but was unsuccessful. We do, however, have the first pair of cemented bifocals made on the prescription of Dr. George M. Gould by Wall and Ochs, in 1888.

Among the pamphlets and papers loaned by Dr. Chance on the history of spectacles was found the photostat of a letter written by Thomas Jefferson to his Philadelphia optician, in which he ordered a pair of bifocals, made to his specifications, similar to those of Benjamin Franklin. He, too, found it necessary to use lenses of different magnifying power and desired both in one frame for convenience.

We have one pair of Eskimo snow spectacles. These are carved from wood and have only a slit for lenses, a protection against snow-blindness.

Before 1843 eyes were not tested for prescription glasses because it was thought that both eyes were alike and a lens that was suited for one eye would suit the other. Therefore, many of the old eyeglasses in our collection have identical lenses, no test for each eye of an individual having been made, but it is surprising, when one slips on a pair of these curious spectacles of our grandfather's day, how very well one can see through them.

There are probably many pairs of old and interesting eyeglasses hidden away in attics and storerooms and long forgotten, some that

differ from any that may be found in the museum. These are the kind that we would like to add to our growing collection, and even if we cannot obtain those used at one time by such distinguished persons as Benjamin Franklin and Thomas Jefferson, if they are unusual or of rare design, or represent some period not already represented, we shall be glad to accept them. So, if at sometime you are disposing of the relics that have accumulated in some old chest or desk drawer, and come across a pair of old eyeglasses, will you please remember the College and the Museum and their Collection of Old Spectacles?

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Adrenalectomy in Relation to Hypertension*

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IN expressing my great appreciation for the invitation to deliver the Fifty-Sixth Mary Scott Newbold Lecture, I do so as a member of a collaborating group, whose work has been accorded this signal recognition and for whom on this occasion I shall attempt to act as spokesman. Drs. W. A. Jeffers, H. A. Zintel, F. D. W. Lukens and J. H. Hafkenschiel, have all been actively engaged in the project to be discussed tonight since its inception and all have played an essential part in whatever progress has been made. Drs. David P. McCallie and A. Gorman Hills joined us later and are now part of our investigative group. Several papers dealing with the earlier phases of the work have been published (1, 2, 3, 4).

Although it is well known that arterial hypertension is one of the two most deadly enemies of life expectancy (the other being atherosclerosis) vital statistics do not fully reflect its lethal effects. Thus, in many cases in which the cause of death is recorded as renal, cardiac or cerebral, these are merely end results of hypertensive disease.

The literature dealing with hypertension is voluminous. According to Smithwick 14,000 articles have been published since 1920 (5). Nevertheless, save in a small minority of cases, we have not yet learned the cause or causes that initiate the hypertensive process, knowledge of the mechanisms by which the blood pressure is maintained at undesirably high levels is imperfect and the results of available methods of treating hypertension often fall far short of our hopes, if not our expectations.

The desirability of learning more than we know about the etiology of arterial hypertension is widely recognized, especially so because of the possibility that further knowledge will furnish important leads toward more effective treatment, both preventive and curative. Despite this lack of knowledge of etiology save in a few special conditions, the possibility now exists that strategic attacks on some part or parts of the mechanism by which hypertension is maintained may lower blood pressure and thus delay or perhaps postpone indefinitely the ravages of the disease. It is to this aspect of the problem that we have directed our chief efforts.

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From the Edward B. Robinette Foundation, Medical Clinic, University of Pennsylvania.

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MECHANISMS BY WHICH BLOOD PRESSURE LEVELS ARE MAINTAINED

The interrelated group of mechanisms which operate to hold the blood pressure level within certain limits and to restore it when it has been moved outside the normal limits furnishes a striking example of the operation of the principle of homeostasis. We have learned that this result is achieved by a complicated system of checks and balances, with summation of effects and antagonisms including compensations for mechanisms that may fail to function efficiently. There is a constant interplay of neurogenic and humoral factors operating upon the hemodynamics of the circulation especially upon cardiac output and the adjustment of arteriolar vasomotor activity. Nevertheless blood pressure can be elevated or lowered in experimental animals by a variety of procedures which alter neurogenic, humoral or hemodynamic functions to a degree such that compensatory functions can no longer maintain homeostasis of pressure.

It seems probable that the etiologic factors concerned in the production of so-called essential and malignant hypertension, whatever they may be, also initiate disturbances in the neurogenic or humoral parts of the blood pressure regulating mechanism which develop to a degree that compensating mechanisms sooner or later fail to maintain the arterial pressure at normal levels. When this occurs it has been suggested that the homeostatic mechanism becomes "set" to maintain pressure in a higher range than normal. This apparently means that the pressure tends to fluctuate from a higher baseline. One might say with equal justification that, in persistent tachycardia, the homeostatic mechanism for heart rate becomes set at a higher level.

In the past, many observers have thought that hypertension is a conservative process designed to ensure adequate blood supply to vital organs and for this reason attempts to lower blood pressure might be injudicious. This teleological view of the benefits of hypertension has not been supported by the course of events when for one or another reason the blood pressure has fallen. Thus, today few would regar hypertension as a useful adjustment save i the presence of special conditions such as ir creased intracranial tension or possibly coarcta tion of the aorta. In most cases, hypertensio may be regarded as an unmixed evil leading t deterioration of arteries and vital organs.

Theoretically, at least, hypertension is ope to attack via the neurogenic, humoral or hemo dynamic factors concerned in its maintenanc or various combinations of these three. Th question to be answered before attemptin such an attack is whether one can make a advantageous trade or series of trades fo hypertension without sacrificing as much as i expected to be gained. The lesions of variou diseases have shown us how hypertension ma be traded for something else although no necessarily to advantage. The effects of ex tensive left ventricular infarction, or upon oc casion an extensive cerebral vascular lesion or the blood pressure levels of hypertensives ma be cited as familiar illustrations.

THERAPY BY INTERFERENCE WITH NEUROGENIC MECHANISMS

The chief therapeutic attacks on the mechanism of hypertension in the past have been attempts to impair the efficiency of neurogenic factors. Most of the drugs used to combat hypertension are supposed to depress neurogenic function at some level ranging from the cerebral cortex down to sympathetic nerve endings. The psychiatrists and more recently a few neurosurgeons have become interested in suprabulbar aspects of elevated pressure. The importance of these approaches to the problem of hypertension is undeniable particularly because of our present regrettable lack of accurate knowledge concerning the role of the cerebral cortex and other structures down to and including the hypothalamus in the initiation and maintenance of the hypertensive process. Other neurosurgeons and some general surgeons have been interested in the "sympatho-adrenal" system by which term they refer to the sympathetic part of the autonomic nervous system and the adrenal medulla. In

recent years much attention has also been devoted to the production of so-called "sympathicolytic" and "adrenolytic" drugs in the effort to block the activity of the sympatho-adrenal system.

The sympatho-adrenal system is the main line of communication from the medulla, where the multitude of neurogenic activities are integrated, to blood vessels throughout the body, so that aside from efferent vagal nerve impulses to the heart, neurogenic control of hemodynamics is exerted almost if not entirely via this system. Because it is accessible to surgery, it has offered a tempting route of attack on hypertension. A variety of operations has been performed. Adson (6) who began with the formidable procedure of bilateral anterior rhizotomy, which was suggested in part by the drop in pressure resulting from spinal anesthesia, finally limited his operation to bilateral removal of lumbar sympathetic ganglia, subdiaphragmatic splanchnicectomy and removal of the coeliac ganglion. Peet (7) removed thoracic ganglia and sectioned the splanchnics above the diaphragm. Grimson's operation is an almost complete bilateral thoraco-lumbar sympathectomy (8). The most widely accepted operation is that of Smithwick (9), which is a bilateral thoraco-lumbar sympathectomy with splanchnicectomy although less extensive than Grimson's operation.

All of the surgeons mentioned above, as well as many other surgeons, have claimed beneficial results from operations upon the sympatho-adrenal system in hypertensives. This aspect of the subject has been studied most extensively by Smithwick. He has classified cases of arterial hypertension into four groups, depending on their severity and has shown that in each group the 5 year postoperative survival rate is better than in cases treated solely by conservative measures (5).

There can be little doubt that sympathectomy has proven of value in the treatment of arterial hypertension. However, in the more severe cases even an operation as extensive as thoraco-lumbar sympathectomy, although it may relieve headache caused by hypertension, arrest the progress of retinopathy and probably prevent transient steep rises in pressure to extremely high levels, usually does not produce a marked fall in blood pressure that extends far beyond convalescence save when the patient is on his feet. Moreover the five year mortality, although better than in non-operated cases, is still high. Medical treatment, even with marked salt restriction or the rice-fruit diet plus the various vasodepressor agents now available, either singly or in combination, although sometimes bringing about gratifying fall in pressure for short periods, frequently fails in the long run even in patients who cooperate to the limit of their ability in burdensome, sometimes almost intolerable restrictions.

It was in the hope that we could help these extremely severe cases of hypertension in which life is threatened by progressive vascular disease involving the brain, heart or kidneys, or by exhaustion of the myocardium through overwork, that we turned to consideration of attacking the humoral mechanism of hypertension. The part of the humoral mechanism most accessible to surgical approach is the adrenal cortex.

Adrenalectomy. The idea that adrenalectomy might be a useful procedure in the treatment of arterial hypertension stems directly from the observation that hypotension is one of the cardinal features of Addison's disease. Even more suggestive is the fact that if a patient with arterial hypertension develops Addison's disease, he not only loses his hypertension but becomes hypotensive. Hypertension has been restored in such patients by the administration of desoxycorticosterone acetate (DCA). However, at least two cases of Addison's disease have been reported in which the blood pressure remained at hypertensive levels probably because of advanced renal disease (10, 11).

So far as we are aware, Crile in 1914 was the first to attempt to treat hypertension by adrenalectomy (12). Other surgeons varied this procedure by slightly more radical adrenalectomy or by combining unilateral adrenalec-

tomy with sympathectomy (13, 14, 15, 16). Good results were reported by these workers, but evidence that would substantiate these favorable opinions has not been presented. More recently, Green, Nelson and Dodds (17) have reported an almost total adrenalectomy in a young woman with extremely severe hypertension and diabetes mellitus. The blood pressure fell to normal levels, symptoms were relieved and the diabetes became less severe. The patient required large amounts of cortical replacement therapy in the early post-operative period but much smaller amounts later (18).

Thoraco-lumbar Sympathectomy and Unilateral Adrenalectomy. At the time the preliminary report of Green's case became available our work had not progressed beyond the planning stage. Our original purpose was to test the assumption that the amount of adrenal cortical activity necessary to maintain hypertension is greater than that necessary to maintain the patient in a state of health. Because cortisone was not available to us at that time and replacement therapy for adrenal cortical deficiency was not entirely satisfactory, it seemed necessary to proceed cautiously. A preliminary step, carried out by Dr. H. A. Zintel, was the removal of an adrenal gland during the second stage of the Smithwick thoraco-lumbar sympathectomy, after having inspected the other adrenal at the first operation. This was done in 17 cases with a view toward later operation on the adrenal gland left in situ provided the results of thoraco-lumbar sympathectomy and unilateral sympathectomy did not prove satisfactory. Thus far we have no evidence to indicate that unilateral adrenalectomy improves the results of thoraco-lumbar sympathectomy, despite previous reports to the contrary (15, 16).

Subtotal Adrenalectomy Subsequent to Thoraco-lumbar Sympathectomy and Unilateral Adrenalectomy. Our first subtotal adrenalectomy was performed in one of these 17 patients, a colored woman 33 years old, on March 21, 1950, nearly a year after the thoraco-lumbar sympathectomy and unilateral adrenalectomy, because her blood pressure had gradually crept up nearly to the pre-operative level and could not be controlled by rigid diet or vasodepressor drugs. On this occasion, approximately 10% of the remaining adrenal gland was left in situ. The operation was well tolerated and only small amounts of aqueous adrenal cortical extract were required to support the patient through the post-operative period. The blood pressure gradually fell to normal levels over the course of the next two months. It has now been in the range of 110 to 120 systolic and 70 to 90 diastolic for one and a half years, in contrast to 220 to 230 systolic and 130 to 140 diastolic before operation. The skin has darkened slightly. So far as we can tell at present, she has completely recovered from the hypertensive disease, without having developed clinical evidence of adrenal insufficiency aside from the slight pigmentation which developed early after operation. We have not tested the possibility of restoring hypertension by administering DCA.

Various Grades of Subtotal Adrenalectomy without Sympathectomy. The course of events in the patient discussed above did not permit us to decide whether the fall in blood pressure had been caused by subtotal adrenalectomy alone or by its combination with thoraco-lumbar sympathectomy. Moreover, although cortisone had become available by this time, so that adrenal cortical insufficiency was no longer as great a hazard as previously, it seemed advisable to ascertain whether we had removed more adrenal tissue than necessary to control hypertension. Subtotal adrenalectomy without section of sympathetic ganglia or nerves was performed in 13 patients with severe, otherwise intractable hypertension, and total adrenalectomy in two patients with severe hypertension and advanced renal disease. From the various procedures carried out in these cases we drew certain conclusions which must be regarded at this time as tentative because of the small number of cases observed. The most important of these conclusions are the follow-

ing: (1) If more than 5% of adrenal tissue is left in situ, there may be little if any effect on the hypertensive level of blood pressure and no evidence of adrenal insufficiency tends to develop except possibly shortly after operation. (2) The attempt to do the entire operation in one stage to save the patient from the hazard of two operations is inadvisable because of the violence of post-operative reaction. It is preferable to leave the adrenal fragment in situ at the first stage operation and remove the other adrenal 10 days later if recovery has been adequate by that time. (3) Adequate amounts of cortisone, fluid and the preservation of a normal electrolyte pattern following the second stage operation tend to prevent serious reactions. (4) Anemia may develop rapidly during the first 10 days after subtotal adrenalectomy has been completed and in some cases may require repeated blood transfusions. (5) The blood pressure does not fall satisfactorily in cases with advanced renal disease. In fact, severe adrenal insufficiency may develop in the presence of hypertension. Thus, the operation is contra-indicated in such cases. (6) Advanced cerebral vascular disease constitutes a serious hazard. Such patients may not stand the operation well, being subject to episodes of encephalopathy following operation and recurrent strokes.

Upon analysis of the cases subjected to subtotal adrenalectomy it was agreed that despite the highly unfavorable material from which not too much could be expected, the results, although promising in some respects, were not satisfactory in most cases. In none had the improvement been as great as in our first patient, although all were older and most had more advanced renal, cerebral or cardiac involvement. Two patients with single stage operations had died within a week as a result of violent post-operative reactions. Two succumbed weeks later to recurrent cerebral vascular seizures. (One patient whose blood pressure was not controlled by operation, died nearly a year later of a cerebral vascular accident). The two patients with advanced renal disease, in whom total adrenalectomy was done, died two to four months after operation, of renal failure, although in one the disease was found to be complicated by periarteritis nodosa, caused possibly by administration of DCA after operation, although it is well known that such vascular lesions may occasionally be found in hypertensives (19). We were most disappointed by the result in a patient with a greatly enlarged heart and a grade III hypertensive retinopathy but only moderately impaired renal function and no clinical evidence of cerebral vascular disturbance. Adrenal cortical insufficiency developed in this patient at high levels of blood pressure. In fact the pressure did not fall until upon one occasion by inadvertence, a severe grade of insufficiency was permitted to develop. Even before this was completely controlled, the blood pressure had again risen to high levels. This was the last case in which subtotal adrenalectomy alone was performed because it had now been demonstrated that even with reasonably good cerebral and renal function, adrenal cortical function could not always be reduced to a level that would satisfactorily control blood pressure. The need for a more efficient operation was therefore obvious. The good result obtained in the case in which both thoracolumbar sympathectomy and subtotal adrenalectomy had been done made it seem desirable to explore further the possibility of a successful attack on hypertension via both humoral and neurogenic mechanisms.

Subtotal Adrenalectomy and Adson-type Sympathectomy. Having convinced ourselves that subtotal adrenalectomy is a relatively ineffective treatment for hypertension when more than 5% of adrenal tissue is left in situ, it was decided that in operations in which adrenal removal and sympathetic nervous system section were to be combined, the fragment of adrenal to be left in situ should not exceed an estimated 5% of a normal amount of adrenal tissue. This is obviously a crude method which necessarily leaves much to the judgment of the operating surgeon. With regard to sympathectomy for hypertension, our preference

had been for the Smithwick thoraco-lumbar procedure. Nevertheless because Adson, on the basis of extensive experience with his more limited procedure, had reported good results (20) and because such an operation adds only slight additional time and little extra trauma, Adson's operation was combined with subtotal adrenalectomy. The operation has always been done in two stages with an interval between operations of nine days or more. Slight modifications have been made in the Adson operation in that (1) no attempt is made to remove the coeliac ganglia, (2) the 12th thoracic ganglion is removed when possible without injuring the diaphragm, and (3) the lumbar ganglia on one side are usually left in situ in younger men, in an effort to preserve satisfactory sexual function.

We are now able to report results of the combined subtotal adrenalectomy and modifications of the Adson type sympathectomy mentioned above in 18 cases, 7 men and 11 women, with post-operative observation ranging in duration from 9 to 5 months. According to Smithwick's classification, 1 patient was in Group I, 5 in Group II, 5 in Group III and 7 in Group IV. The age range was 16 to 56 with 1 patient in the second decade, one in the third, 2 in the fourth, 10 in the fifth and 4 in the sixth.

Two deaths have occurred thus far in this series of 18 cases. One resulted from uremia 5 months after operation. The patient, a 52 year old woman, had been recognized as a poor risk because of impairment of renal function. The other patient who died, a 41 year old woman, had undergone a hemiplegic attack prior to operation but had made a satisfactory recovery. After operation, the blood pressure fell from high levels to a normal range and she was regarded as greatly improved. Five months after operation, without known antecedent symptoms, she was found dead in bed one morning. Necropsy was not performed and the cause of death, therefore, not established. All of the other patients derived at least some benefit from the operation. In 8, the blood pressure is usually found to be within the normal range. In 7, the pressure has been materially lowered but, in most readings, not to a normal range. The poorest result was obtained in our youngest patient, a 16 year old girl with extremely high levels of both systolic and diastolic pressure and severe intractable headaches. Although she was completely relieved of headaches and felt well after operation, the fall in blood pressure was slight. Despite the fact that only a small fragment of one adrenal was left in situ, estimated to be little more than 5% of the gland, she has never exhibited evidence of adrenal cortical insufficiency, a course of events which suggests the presence of a functioning cortical rest. One other patient in this series had been one of our poorer results following subtotal adrenalectomy alone, although severe headaches had been relieved following that operation. Our failure to obtain a satisfactory fall in pressure had been attributed at least in part to the probability that not enough adrenal tissue had been removed. Approximately 10% of each gland had been left in situ and no evidences of adrenal insufficiency had occurred. However, prior to operation, cerebral flow studies had revealed an extremely high cerebral vascular resistance, the importance of which, as a possible cause of the disappointing result, we were unable to evaluate. In any event, the possibility that advanced cerebral vascular disease had contributed to our inability to lower pressure materially could not be excluded. In view of the prospect of further rapid vascular deterioration because of extremely high blood pressure in this patient, it was decided to perform a bilateral Adson type sympathectomy and in addition to remove at least one of the adrenal fragments if it could be found at operation. During one of the operations the vascular supply of a kidney was damaged and the kidney was therefore removed (found later to present an astonishingly normal histological appearance). The adrenal fragment was not found at the first operation nor could it be demonstrated in tissue removed in the hope that the fragment would be included. An attempt to find the fragment on the other side

was similarly unsuccessful. Nevertheless, the blood pressure promptly fell from extremely high levels to normal and the patient now required replacement therapy, which after the early post-operative period has been 12.5 mg. cortisone daily. Since the second pair of operations he has continued to improve and for several months has been working about half time. This patient and a more recent one, not included in this series, have demonstrated that advanced cerebral vascular disease, although, as stated above, a serious hazard, does not necessarily prevent a good result and that marked improvement in cerebral function may occur after the blood pressure falls.

The most spectacular improvements have occurred in patients with congestive heart failure. There have now been 9 such patients operated upon, in 3 of whom subtotal adrenalectomy alone was performed, and in 6, the combination of subtotal adrenalectomy and Adson type sympathectomy (3 too recent to be included in the present series). All of these patients had required severe limitation of activity, salt restriction, digitalis, and mercurial diuretics usually at frequent intervals prior to operation. Some, even with the most careful management, could not avoid congestive phenomena. All improved rapidly after the second operation. The 6 included in this report require no therapy for heart failure and no restriction of activity, or salt intake. The three more recent cases still receive small amounts of digitalis, although they no longer appear to need it. It seems probable that the relief of heart failure has depended not only on lowering of blood pressure, but also on the effect of lessened adrenal function upon water and electrolyte excretion.

DISCUSSION

The work done and the observations made to date constitute only the beginning of an undertaking that will require the labor of many investigators over a long period of time before being completed. At present we know nothing concerning the long term results of the procedures that have been carried out. The short term results, however, have been most promising from the viewpoint of fall in blood pressure, relief of hypertensive type headache, relief of heart failure, decrease of cerebral vascular resistance (21), improvement of renal plasma flow (22), and rehabilitation of patients. In most of the patients in whom the fall in pressure following operation was not as great as was desired, increased susceptibility to some of the newer vaso-depressor drugs has been demonstrated (23).

We have not succeeded in a single case in which adrenalectomy alone was performed in achieving our objective of a normal blood pressure without the need for adrenal cortical replacement therapy. The nearest we have come to this has been in a patient whose blood pressure levels fell to normal, but who appears to require no more than 3 to 6 mg. cortisone daily. There seems little doubt that we would have obtained more good results in this series of cases if we had carried out total adrenalectomy routinely, a procedure undertaken by Thorn (24), after our work was under way. Total adrenalectomy has one point of superiority over the subtotal procedure in that the hazard of not removing enough adrenal tissue to obtain a good result is eliminated (save in possible exceptional cases in which an adrenal cortical rest might be able to carry on adequate function). If, however, we had not carried out various degrees of subtotal adrenalectomy, we would not have data to ascertain (1) how much adrenal can be removed in the human, without loss of normal adrenal function, and without material influence upon hypertensive levels of blood pressure, and (2) that the range between the amount of adrenal function necessary for the well-being of a patient and that required to maintain a hypertensive state, if it exists at all, is so narrow that only by a lucky accident could one relieve hypertension without creating the need for replacement therapy. The poor results obtained by total adrenalectomy in our two cases with serious renal impairment support Thorn's belief that in "severe progressive advancing renal impairment" the modifying influence of the adrenal cortical

hormones becomes increasingly less important. The explanation of our poor results, however, in two cases without much renal impairment and with enough adrenal removed so that some replacement therapy was required, is not so easy. We have not ruled out the possibility in these cases that a better result might have been obtained by complete adrenalectomy and complete replacement therapy. The possibility that a satisfactory replacement combination can be found with less pressor effect than the secretion of the patient's own adrenal cortex does not seem too remote.

At present, there is little reason to believe that the adrenal gland plays any part in the etiology of the hypertensive state, save in special conditions such as pheochromocytoma. That its function is necessary for the maintenance of hypertension in most cases except those with advanced renal disease, seems well established. Recent studies by Dohan and Richardson in our patients appear to indicate that patterns of corticoid excretion may differ (25). Whether it follows from this that the secretion of some adrenals is more vasopressor than that of other adrenals and that the results of adrenalectomy can be predicted on such a basis must await future developments in the study of adrenal cortical activity.

It is probably erroneous to think that effects of neurogenic and humoral factors on blood pressure are as disparate as the discussions by writers on these subjects would appear to indicate. Our attention was drawn to the possibility of summation of effects resulting from interference with neurogenic and humoral mechanisms by the observations in our first patient on whom subtotal adrenalectomy was completed after thoraco-lumbar sympathectomy and unilateral adrenalectomy had failed to reduce the blood pressure satisfactorily. This patient lost the postural hypotension that developed after thoraco-lumbar sympathectomy, but it returned promptly after subtotal adrenalectomy. In our fourth patient the blood pressure had not been lowered materially by a Peet type sympathectomy several years previously. Following a subtotal adrenalectomy, which we now know was inadequate, he developed no evidences of adrenal insufficiency, and only a modest fall in blood pressure. However, for the first time he exhibited a sharp fall in pressure when he stood. Later we were to find that subtotal adrenalectomy alone, even when extensive enough to produce adrenal insufficiency, does not usually cause persistent postural hypotension. There is obviously more than one possible reason why adrenalectomy might potentiate a postural hypotension, the basis for which had been established by splanchnicectomy, but an hypothesis deserving consideration is that adrenalectomy may be effective in combatting intrinsic vasoconstriction even though it may not prevent the constriction initiated by sympathetic nerve activity.

Medical knowledge has come not from deep abstract thinking, which merely means building too many assumptions upon hypotheses, but by careful observation, the construction of hypotheses that appear to account for facts, then tests of such hypotheses, their reconstruction in the light of what happened when they were tested and so on. We are in the midst of such a process now in an effort to control hypertension. We have gone far enough to become convinced that hypertension can be controlled, although at this time we do not know what the ultimate methods of control will be. Pending further knowledge, the most effective attack on severe, otherwise intractable hypertension now available is the combination of subtotal adrenalectomy and sympathectomy. There need no longer be fear of producing adrenal insufficiency. Thanks to modern management, it may be accepted with great advantage when necessary in the trade for hypertension provided vigilance is constantly exercised. During the time surgical methods are being perfected, the principle of simultaneous attacks on various parts of the mechanism by which hypertension is maintained would appear to deserve attention in medical investigation. The development of medical procedures that would achieve the same objectives as

those now attained by surgery would obviously take precedence.

Perhaps a word should be said in behalf of the great army of hypertensives, who march on year after year enjoying freedom from symptoms, able to carry on normal activities, who show little evidence of vascular or myocardial deterioration as time goes on. We know they are not first class life insurance risks because vitally important blood vessels subject to the stress of hypertension do give out now and then. However, it hardly seems reasonable to make these hypertensives miserable by denying them all the things that make life endurable. A physician would be neglectful of his duty if he did not encourage them to observe the ancient maxim of moderation in all things, which we are taught should lead to happiness rather than the reverse. It is only when the danger signals begin to fly and calamity is in the offing that measures such as those discussed above should come under consideration.

Summary

1. Studies have been undertaken to ascertain whether subtotal adrenalectomy is of value in the treatment of severe otherwise intractable arterial hypertension.

2. It has been found that in order to reduce adrenal function to a degree that the blood pressure will fall from hypertensive levels, at least 90% and sometimes more than 95% of adrenal tissue must be removed. When this is done evidences of adrenal cortical insufficiency may develop and require treatment. The range between the amounts of replacement therapy required to avoid both cortical insufficiency and hypertension is at best narrow. In fact, in some patients it may not be possible to reduce replacement therapy to a degree that will permit the blood pressure to fall to a satisfactory level.

3. The combination of subtotal adrenalectomy and thoraco-lumbar sympathectomy, or even a less extensive sympathectomy such as the Adson type, has been a more efficient method of lowering blood pressure than subtotal adrenalectomy alone. Cerebral vascular resistance tends to be lowered, renal plasma flow increased and cardiac failure relieved. Relief of symptoms has occurred in nearly all patients. Thus far all who had been made invalids by cardiac failure have been rehabilitated.

4. The indications and contraindications for operation, the post-operative management, and mortality have been discussed.

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Dr. F. Curtis Dohan and Dr. E. M. Richardson have carried out the studies of corticoid and 17-ketosteroid excretion.

Miss Nelly Jane Keffer has made daily blood pressure readings when patients were in the hospital, including postural tests whenever possible. She has helped prepare various tables.

Generous supplies of adrenal cortical extract have been furnished by the Upjohn Company.

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Ciba Company has furnished DCA for both oral and parenteral use.

The Schering Company has supplied DCA for both oral and parenteral use.

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Transactions of the Sections

SECTION ON GENERAL MEDICINE

28 May 1951

THE CLINICAL EXPRESSIONS AND THERAPEUTIC AVENUES OF MÉNIÈRE'S DISEASE. Maurice Saltzman*, M.D. (Discusser: N. W. Winkelman, M.D.) (*Abstract 1, below*)

THE MORTALITY OF ACUTE MYOCARDIAL INFARCTION TREATED AT HOME. Samuel Baer*, M.D., William I. Heine*, M.D., and Sidney O. Krasnoff*, M.D. (Discusser: Louis B. Laplace, M.D.) (*Abstract 2, below*)

TRICHINOSIS IN THE PHILADELPHIA AREA. Julian Love*, Capt., M.C., U.S.N., Boyd K. Black*, Lt. Com., M.C., U.S.N., and Thomas J. Anderson*, Lt.(jg), M.C., U.S. N.R. (Discusser: Martin P. Crane, M.D.) (*Abstract 3, below*)

THE EFFECT OF SERUM FROM INSULIN-RESISTANT CASES ON THE COMBINATION OF INSULIN WITH RAT DIAPHRAGM. Julian B. Marsh, M.D., Niels Haugaard*, Ph.D., and William C. Stadie, M.D. (Discusser: F. Curtis Dohan, M.D.) (*Abstract 4, below*)

22 October 1951

A NEW DEVICE FOR STEREOSCOPIC CEREBRAL AND CARDIAC ANGIOGRAPHY. W. Edward Chamberlain, M.D., and Herbert M. Stauffer*, M.D. (Discusser: J. Stauffer Lehman*, M.D.) (*Abstract 5, below*)

THE EVALUATION OF PATIENTS FOR COMMISSUROTOMY. George D. Geckler*, M.D., and Lowell L. Lane*, M.D. (Discusser: Harry F. Zinsser*, M.D.) (*Abstract 6, below*)

HYDROCORTISONE (COMPOUND F) AS A LOCAL ANTI-INFLAMMATORY AGENT. Joseph L. Hollander, M.D., and E. M. Brown, Jr.*, M.D. (Discusser: John Lansbury, M.D.) (*Abstract 7, below*)

STUDIES ON PREGNANCY IN ADDISON'S DISEASE. K. E. Paschkis, M.D., J. J. Rupp*, M.D., and J. J. Schneider*, M.D. (Discusser: William H. Pearlman*, Ph.D.) (*Abstract 8, below*)

26 November 1951

THE TREATMENT OF ULCERATIVE COLITIS WITH ACTH. C. Wilmer Wirts, M.D., and Herbert A. Yantes*, M.D. (Discusser: Thomas Johnson, M.D.) (*Abstract 9, below*)

OBSERVATIONS ON THE COINCIDENCE OF GOUT AND DIABETES. Elliott F. Maguire*, M.D., and Robert Gill*, M.D. (Discusser: Francis D. W. Lukens, M.D.) (*Abstract 10, below*)

INTERMITTENT CLAUDICATION IN EXTREMITIES WITH NORMAL CIRCULATION. Meyer Naide, M.D. (Discusser: Nicholas Padis, M.D.) (*Abstract 11, below*)

THE ASYMPTOMATIC CARRIER STATE IN INFECTIOUS (VIRAL) HEPATITIS. J. Edward Berk, M.D., Joseph Stokes, Jr., M.D., Miles Drake*, M.D., Leonard L. Malamut*, M.D., R. B. Capps*, M.D., and Werner Henle*, M.D. (Discusser: John R. Neefe, M.D.) (*Abstract 12, below*)

SECTION ON MEDICAL HISTORY

Fourth Series of Lectures for Medical Students

I. INTRODUCTORY: THE MEANING AND VALUES OF MEDICAL HISTORY. Richard H. Shryock*, Ph.D. (15 October 1951)

II. CLASSICAL AND MEDIEVAL MEDICINE. Owsei Temkin*, M.D. (22 October 1951)

III. RENAISSANCE MEDICINE. DR. TEMKIN. (29 October 1951)

IV. 17TH AND 18TH CENTURY MEDICINE. Dr. Temkin. (5 November 1951)

V. 19TH AND 20TH CENTURY MEDICINE. Dr. Shryock. (12 November 1951)

VI. SOCIAL ASPECTS OF MEDICAL HISTORY. Dr. Shryock. (19 November 1951)

* By invitation.

SECTION ON OPHTHALMOLOGY[1]

18 October 1951

MIXED CELL TUMOR OF THE LACRIMAL GLAND: CASE PRESENTATION. Charles G. Steinmetz, 3d*, M.D.

THE CONSIDERATION OF THE END RESULTS OF A NUMBER OF CASES OF CYCLO-DIATHERMY. E. I. Rubin*, M.D., J. Romig*, M.D., and J. H. Malloy*, M.D.

THE USE OF SURFACE THERAPY WITH THE THERMOPHORE IN THE TREATMENT OF RETINAL DETACHMENT. Edward S. Gifford, Jr., M.D.

15 November 1951

TONOGRAPHIC STUDIES OF EARLY GLAUCOMAS. Peter C. Kronfeld*, M.D. (*Fourteenth Annual de Schweinitz Lecture.*)

20 December 1951

MALIGNANT MELANOMA OF THE CILIARY BODY: CASE REPORT. Paul A. Rockwell*, M.D. (Discusser: Dr. A'Valdes-da Pena*)

THE OCULAR LESIONS OF LEPROSY. P. J. Kennedy, M.D. (Discusser: J. V. Klauder, M.D.)

INTRA-OCULAR PENETRATION OF CORTISONE. Irving H. Leopold, M.D., Florian Maylath*, M.D., and C. Steinmetz*, M.D.

[1] Abstracts of the presentations at this Section customarily appear in the *American Journal of Ophthalmology* and the *Archives of Ophthalmology.*

SECTION ON OTOLARYNGOLOGY[2]

21 November 1951

THE ORGAN OF CORTI AS WE SEE IT TODAY, ONE HUNDRED YEARS AFTER ITS DISCOVERY. Dorothy Wolff*, Ph.D. (Discusser: Oscar V. Batson, M.D.)

DEMONSTRATION OF THE MÜTTER MUSEUM'S POLITZER COLLECTION OF TYMPANIC MEMBRANES AND HYRTL COLLECTION SPECIMENS SHOWING THE COMPARATIVE ANATOMY OF THE INNER EAR. Douglas Macfarlan, M.D.

19 December 1951

FURTHER CLINICAL INVESTIGATION OF THE EFFECT OF DRAMAMINE UPON THE COCHLEAR FUNCTION. Julius Winston, M.D., and Joseph Sataloff*, M.D. (Discusser: Edward H. Campbell, M.D.)

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

23 November 1951[3]

MULTIPHASIC HEALTH EXAMINATIONS. E. M. Holmes, Jr.*, M.D.

NEWER PROBLEMS IN THE EPIDEMIOLOGY OF PULMONARY DISEASE. Harold L. Israel, M.D.

[2] Abstracts of the presentations at this Section customarily appear in the *Archives of Otolaryngology.*

[3] Joint meeting with Region No. 1 of the Pennsylvania Public Health Association.

ABSTRACTS

Abstract 1

THE CLINICAL EXPRESSIONS AND THERAPEUTIC AVENUES OF MÉNIÈRE'S DISEASE. Maurice Saltzman, M.D.

Ménière's disease is an inner ear disturbance with the cardinal symptoms of vertigo, deafness and tinnitus.

Clinical forms comprise:

1. Apoplectiform. Histo-Pathology—hemorrhage in the static labyrinth. Etiology—leukemia.

2. Endolymphatic hydrops. Histo-Pathology—localized edema in scala media. Theories as to etiology—(a) Allergy (b) Abnormal water and electrolyte metabolism (c) Vasomotor disturbance.

3. Endolymphatic hydrops without vertigo but with the characteristic pattern of deafness.

4. Symptomatic Ménière. The labyrinthine symptoms are secondary to disease elsewhere in the body.

5. Psychosomatic Ménière. The mechanism is anxiety neurosis.

Therapeutic Avenues:

1. Surgery—intractable case.

2. Medical Treatment: (a) Elimination of sodium and administration of potassium. Efficacy and rationale not proven; (b) Histamine desensitization—contrary to latest concept that histamine desensitization cannot be accomplished; (c) Vasodilators. Histamine and nicotinic acid are best; (d) Histamine intravenously. Dramatic results reported.

Abstract 2

THE MORTALITY OF ACUTE MYOCARDIAL INFARCTION TREATED AT HOME. Samuel Baer, M.D., William I. Heine, M.D., and Sidney O. Krasnoff, M.D.

Representative published studies on the immediate mortality of acute myocardial infarction have indicated death rates varying from 8% to 51%, the majority being in the neighborhood of 20%–35%. In our review of 1220 cases admitted to one hospital in Philadelphia from 1934 to 1950, the annual mortality ranged from 51% to 21%, with an overall fatality rate during hospitalization of 34%. From our experience with patients seen at home, however, we questioned whether the prognosis of acute myocardial infarction was as poor as it seemed from hospital statistics and published mortality studies.

Reviewing 3200 electrocardiograms taken by one of us in private practice from 1939 to 1950, we selected 182 cases which met rigid electrocardiographic criteria for the diagnosis of acute myocardial infarction. The clinical picture in each patient was consistent with the diagnosis. All were originally seen at home or in the office, 51% in the first 3 days and 83% in the first week of their disease. Age incidence, sex ratio, and localization of the infarctions corresponded closely to the distribution of these factors in our previous studies and in other reports in the literature. Of these 182 patients, treated by 67 physicians, 16 died during the first 6 weeks of their illness, a mortality rate of 8.5%. Only 4% received dicoumarol.

The mortality rate in this series compares favorably with the lowest reported in the American literature, including that of the Committee for the Evaluation of Anticoagulants. The advisability of routinely hospitalizing all patients with acute myocardial infarction seems questionable. The economic implications are obvious. We feel that the ominous prognosis associated with acute myocardial infarction by most laymen, and even some physicians, is unjustified.

Abstract 3

TRICHINOSIS IN THE PHILADELPHIA AREA[4]. Julian Love, CAPT., M.C., U.S.N., Boyd K. Black, LT. COM., M.C., U.S.N., and Thomas J. Anderson, LT.(jg), M.C., U.S.N.R.

1. The occurrence of trichinosis in the Philadelphia area has been demonstrated by the occurrence of eight cases in the U. S. Naval Hospital, Philadelphia in the past two years.

2. This infestation should be of interest to Philadelphians because Dr. Joseph Leidy of this city was the first to demonstrate the larvae in microscopic study of infected ham and, thereby, proved the transmission of the disease in 1846.

3. That the disease can be fatal is emphasized by a death that occurred in an Orthodox Jewish male in this series, and another such fatality is described in a recent issue of a popular lay magazine.

4. Effective public health measures for the eradication of the disease have been available for many years, but such measures are not fully employed by even our large meat packing concerns.

5. The clinical picture, history, outstanding symptoms and physical findings in the eight patients have been described. Eosinophilia and muscle biopsy are the most practical and reliable means of verifying the diagnosis. Postmortem study of Case No. 1 and pertinent sections of muscle tissues of three other patients were exhibited.

6. Treatment, heretofore, has been supportive and symptomatic but it is suggested that Diethylcarbamazine (Hetrazan Lederle), an ef-

[4] The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

fective nematocide for filariasis and creeping eruption, be tried as scattered reports indicate it may be of value.

Abstract 4

THE EFFECT OF SERUM FROM INSULIN-RESISTANT CASES ON THE COMBINATION OF INSULIN WITH RAT DIAPHRAGM. Julian B. Marsh, M.D., Niels Haugaard, PH.D., and William C. Stadie, M.D.

When an isolated rat hemidiaphragm is exposed to a solution of insulin for one minute, it synthesizes more glycogen than its paired control. In the presence of serum from insulin-resistant patients, the effect of insulin in promoting glycogen synthesis was found to be diminished. This may be due to inactivation of the insulin by some factor present in serum from insulin-resistant persons. The extent of the insulin-neutralizing effect of serum was roughly correlated with the clinical severity of the insulin resistance.

Abstract 5

A NEW DEVICE FOR STEREOSCOPIC CEREBRAL AND CARDIAC ANGIOGRAPHY. W. Edward Chamberlain, M.D., and Herbert M. Stauffer, M.D.

In the past few years angiocardiography and cerebral angiography have come to be widely employed in roentgen diagnosis. The stereoscopic angiographic device was designed with the following rather rigorous group of criteria in mind:

1. Rapid serial angiography
2. Exposures in two planes simultaneously

In the past it has been necessary to make an additional injection of contrast material to secure the films in a second plane.

There are important objections to the use of more than one injection. Neither cerebral angiography nor angiocardiography is without hazard. For cerebral angiography the most widely used method at the moment is the percutaneous injection into the common carotid artery of about 10cc of 35% diodrast or similar organic iodine compound. Broman and Olsson have shown that higher concentrations of diodrast or prolonged administration will destroy the blood-brain-barrier transiently or permanently in experimental animals. Convulsions, hemiplegia and occasionally death are complications which may be decreased by minimizing the number of injections.

In angiocardiography in adults 50cc of 70% diodrast is usually injected in 1½ seconds into an ante-cubital vein. Dotter recently collected reports on mortality in almost 7000 angiocardiographic studies; there were 23 deaths attributable to the usual technique; 11 patients died following a single injection, 9 died following two injections, and 3 following a third injection. Half of the deaths might have been avoided had a second injection not been required.

3. Stereoscopic exposures
4. Flexibility

The apparatus was designed for use with the patient either in the horizontal or vertical position.

The device in its final form consists of two rapid-sequence roll-film cassettes mounted in a large circular frame with the two roentgen tubes at right angles to each other; a motor drive produces the necessary stereoscopic tube shift between each pair of right angle exposures which are secured at the rate of two per second.

Abstract 6

THE EVALUATION OF PATIENTS FOR MITRAL COMMISSUROTOMY. Geo. D. Geckler, M.D., and Lowell L. Lane, M.D.

Mitral Commissurotomy has become an accepted procedure in the treatment of mitral stenosis. The selection of patients for this operation is the important responsibility of the cardiologist.

Basic considerations include the following:
1. Does the patient have an operable lesion?
2. Is the patient a satisfactory operative risk?
3. Does the degree of anticipated benefit warrant the risk of the operative procedure in the individual case?

Numerous factors are involved in the evaluation of candidates. Active rheumatic infection is an absolute contraindication. Patients over

50 years of age are usually unacceptable. The lesion should preferably be a "pure" mitral stenosis with insufficiency minimal or absent. An associated aortic lesion, if predominant or well advanced, renders operation undesirable. Marked cardiac enlargement is a definite contraindication. Patients with atrial fibrillation are acceptable.

A history of progressive impairment of functional capacity is essential. The mere presence of a mitral diastolic murmur is not sufficient reason for operation. Unalleviable chronic congestive failure is usually a contraindication. Patients with history of hemoptysis or embolic episodes are often acceptable. Emotionally unstable individuals are undesirable candidates regardless of cardiac considerations. The desire of the patient for operation should not influence the decision of the cardiologist.

Abstract 7

Hydrocortisone (Compound F) as a Local Anti-inflammatory Agent. Joseph L. Hollander, M.D., and E. M. Brown, Jr., M.D.

Injected locally, compound F (hydrocortisone) is much more effective than cortisone in suppressing the synovial inflammation of rheumatoid arthritis. The reason for this difference is unknown.

Nearly 700 injections have been given into the joints of 129 patients without untoward effects.

In 69 patients with rheumatoid arthritis, injection of hydrocortisone into one or more joints has resulted in prompt local alleviation of symptoms and signs. The completeness of improvement has varied considerably, and the duration of benefit has varied from a few days to several weeks.

In 39 patients with osteoarthritis, injections of hydrocortisone into one or more joints has resulted in prompt relief of symptoms and signs. There has been greater relief for longer periods in this condition than observed in rheumatoid arthritis.

Preliminary trials with hydrocortisone locally in various forms of bursitis, gouty arthritis, disseminated lupus erythematosus, traumatic arthritis, and ocular inflammations complicating rheumatoid arthritis have been encouraging.

There has been an absence of systemic effects and adverse reactions from this local method of utilizing hydrocortisone, and cessation of injections has not been followed by exacerbations of the local inflammation.

These observations suggest that the local administration of hydrocortisone may be of practical value in the management of certain local inflammatory states.

Abstract 8

Studies on Pregnancy in Addison's Disease. K. E. Paschkis, M.D., J. J. Rupp, M.D. and J. J. Schneider, M.D.

The case of a 39 yr. old colored woman is presented who was first seen in impending Addisonian crisis. Following emergency therapy she was treated with desoxycorticosterone acetate and NaCl. 4–6 weeks after discharge from the hospital she became pregnant. Re-admission because of impending crisis due to vomitus of pregnancy. Management was difficult during the first 4 months because of severe vomitus. Subsequent course rather uneventful until 8th month when a large pleural effusion with high fever (probably activation of old T.b.) occurred. Treatment with D.C.A., salt and cortisone is briefly outlined. Delivery at term, under appropriate hormonal treatment, well tolerated and uneventful. Normal healthy baby.

Formaldehydogenic steroids before pregnancy were 289γ/24 hrs., a low value to be expected in Addison's disease. In the 4th month a single excretion value of 742γ/24 hrs. was obtained, in the 6th month values ranged from 440 to 510γ. In the 6th month a drop of blood eosinophils of 56% following epinephrine injection, and of 57% following injection of 25 mg. ACTH was observed. Curiously, treatment with 100 mg. of ACTH for one week resulted not in a rise, but a decrease of formaldehydogenic steroids, accompanied by a gradual rise of the circulating eosinophils. These observations suggest that "corticoids" were elaborated in tissues other than the adrenal, presumably

in the placenta. A similar observation by J. Jailer is quoted. In the case presented here, the placenta was extracted but no "corticoid" material was obtained. Haines however has found "corticoid" steroids upon extraction of large amounts of placental tissue.

Abstract 9

THE TREATMENT OF ULCERATIVE COLITIS WITH ACTH. C. Wilmer Wirts, M.D., and Herbert A. Yantes, M.D.

We have employed ACTH in the treatment of 16 patients with idiopathic ulcerative colitis at the Jefferson Hospital. During treatment all showed defervescence, cessation of diarrhea, increase in appetite, improvement in the emotional state, weight gain and correction of anemia. From this study ACTH appears to be a potent form of adjunct therapy, but previously recognized forms of treatment are still necessary and should be used as clinical judgment dictates.

Remission of the colitis can occur up to 16 months, but we do not feel that the underlying disease is cured, because no patients have shown a complete return to a normal proctoscopic appearance of the bowel. Also many patients continue to have some abnormality in bowel function and relapse may still occur in any of them.

It appears that doses as small as 20 mg. ACTH every 12 hours intramuscularly for 2 to 3 weeks may be sufficient to cause a cessation of symptoms. If improvement is not noted in 48 to 72 hours the dose should be increased when given intramuscularly, or the intravenous route may be tried. When given intravenously we have used 15 mg. ACTH in 500 c.c. of 5% glucose administered over an 8 hour period. It is desirable to use the smallest effective dose to avoid side effects and reduce expense.

Abstract 10

OBSERVATIONS ON THE COINCIDENCE OF GOUT AND DIABETES. Elliott F. Maguire, M.D., and Robert Gill, M.D.

It is recorded that the concurrence of gout and diabetes has not heretofore attracted the attention of most of the contemporary American physicians. European authorities of the last century, however, were convinced of a distinct inter-relationship between gout and diabetes. References are noted. The striking clinical similarities between gout and diabetes that have been known for many years are outlined.

The recent clinical ward experience at the Pennsylvania Hospital is reviewed. All admissions to the Pennsylvania Hospital for a three year period beginning January 1, 1948 and ending December 31, 1950 were considered. During this period 17,401 patients were admitted and of these 550 (3.2%) were diabetics and 34 (0.2%) were gouty. There were six cases of concurrent gout and diabetes. Thus it was noted that gout was observed in 1.1% of all diabetic admissions and diabetes was observed in 18% of all gouty admissions. It is noted that the incidence of gout in the diabetic population is six times as great as may be expected by chance alone.

Interesting clinical features of the six patients with concurrent diabetes and gout are recorded.

The current literature in experimental medicine is briefly reviewed and support is found for the clinical impression of an inter-relationship between gout and diabetes. It is noted that diabetes has been produced in animals by the intraperitoneal injection of uric acid. Attention is also called to the fact that visceral gout appeared in pigeons associated with the diabetes produced by alloxan.

A hypothetical biochemical mechanism is presented to explain the development of diabetes in gouty patients.

Abstract 11

INTERMITTENT CLAUDICATION IN EXTREMITIES WITH NORMAL CIRCULATION. Meyer Naide, M.D.

The term intermittent claudication has become synonymous with reduced blood supply to muscle. The symptom is said to always indicate an inadequate supply of arterial blood to contracting muscles (Allen, Barker and Hines). It is brought on only by continuous exercise and relieved promptly by stopping the exer-

cise. There is a group of patients, however, who have typical intermittent claudication in whom no evidence can be found of reduced blood supply to the leg muscles. A study of such patients discloses evidence that the claudication is probably the result of spine or cord conditions. Signs in some of the patients suggest lumbo-sacral disease such as probable discs with root pressure. Ischemia to roots or the lumbar cord as the result of primary arterial disease or due to pressure as the result of prolapsed or degenerated discs may be responsible for intermittent claudication in some patients. Other patients seem to have the symptom on the basis of neuropathy due to diabetes mellitus or to pernicious anemia. This group of patients must be differentiated from the usual type, since the cause is not thromboangiitis obliterans or arteriosclerosis in the vessels of the legs.

Abstract 12

THE ASYMPTOMATIC CARRIER STATE IN INFECTIOUS (VIRAL) HEPATITIS. J. Edward Berk, M.D., Joseph Stokes, Jr., M.D., Miles Drake, M.D., Leonard L. Malamut, M.D., R. B. Capps, M.D., and Werner Henle, M.D.

Accumulated knowledge regarding the epidemiology of serum transmitted viral hepatitis strongly suggests the existence of a carrier state in this disease. To date, however, no long-term asymptomatic carrier has been demonstrated. This report is concerned with clinical observations and experimental transmission studies in three subjects establishing for the first time the existence of asymptomatic carriers of serum hepatitis.

The first subject, a professional blood donor, was a chronic alcoholic with demonstrated chronic liver disease. He was entirely asymptomatic, had never been jaundiced and denied any earlier episode suggestive of infectious hepatitis. Four of a group of 12 patients who had survived 40 or more days after transfusion with his blood were found to have developed hepatitis with jaundice. Blood obtained from this donor approximately 5½ years after transfusion of the first identified case of serum hepatitis among his recipients, produced hepatitis when inoculated into human volunteers.

The second subject, a young mother, was asymptomatic and gave no history suggesting hepatitis in the past. The liver appeared to be normal on physical examination and was functionally intact as shown by liver function tests. She had been delivered of a normal baby by cesarean section and the baby was not breast fed. Development of the infant proceeded normally until 2 months of age when hepatitis with jaundice appeared. This progressively worsened and eventually resulted in death of the child at 16 months of age. Both the baby's and mother's blood, obtained when the baby was 9 months old, induced hepatitis when injected into human volunteers. Blood was taken again from the mother 2 years and 11 months after birth of the infant. During this time she had remained well and hepatic function tests performed at the time blood was drawn were again normal. Injection of this blood into human volunteers demonstrated that it was still capable of transmitting hepatitis.

The third subject, a veteran of World War II, appeared clinically to be entirely well. He gave no history to suggest previous hepatitis although he had had malaria while a prisoner of war. Physical examination was negative. Liver function tests disclosed an abnormal thymol turbidity test, an equivocally abnormal zinc sulfate turbidity test, and serum alkaline phosphatase activity just over normal. Three patients who had been transfused with his blood each developed hepatitis with jaundice. Transmission experiments conducted on human volunteers with blood drawn from this donor some 10 months after the first of the clinical recipients had been transfused, proved that it still possessed the ability to transmit hepatitis.

These observations clearly demonstrate the existence of chronic asymptomatic carriers of serum hepatitis. Since no suitable means of clinically detecting such carriers is currently available, there is an obvious need for an effective method of inactivating hepatitis virus in all donor blood.

President's Address*

By T. GRIER MILLER

THIS COLLEGE is a unique organization. Although incorporated in 1789 as a "literary institution", its objectives as stated in its charter included many types of medical activity: research, the cultivation of "order and uniformity in the practice of physic" and the recording of medical observations at home and abroad. With the subsequent development of medical schools in this country and later of institutions devoted entirely to investigation, medical research soon was largely relegated to them. With the organization of county, state and national medical societies, as well as the intrusion of governmental agencies into the field, the regulation of medical practice became one of their chief functions. Consequently neither research, in the modern sense, nor the supervision of practice, nor even the undergraduate teaching of medicine, has ever been a primary function of this College. As a recorder and disseminator of medical observations, however, it has always measured up to the requirements of its charter. Indeed, in making available to the profession and to the public a great medical library and a forum for the presentation and discussion of current medical problems, it has afforded an essential background for research, teaching and practice, and so fundamentally, though indirectly, has contributed to all its original objectives.

The service that the College can render in the future will depend on the extent to which it continues to meet the need for a steadily enlarging depository of medical knowledge, on the facilities it continues to provide for making that knowledge easily available to the profession and the public and on the opportunity it affords for the free and unprejudiced presentation and discussion of medical problems. To implement these objectives, more building space and more adequately remunerated personnel are required.

In order to emphasize the future needs of the College, allow me briefly to review some of its activities for the past three years and to state its present situation. During that period I have been its president, and it has been a happy experience, but I appreciate that much of what was anticipated in 1949 has not been realized. And yet it may be recorded that the number of Fellows has increased slightly, that an executive secretary and an administrative assistant librarian have been added to the staff, that a pension system has been established for its employees and their wages modestly increased, and that almost $90,000, largely from the Fellows themselves, has been secured for a new building and endowment fund.

Fellowship

The total Fellowship at the beginning of 1949 numbered 829: 757 of Resident, 61 of Non-Resident and 11 of Honorary status. Now the total is 877, of whom 796 are Resident Fellows. During the three years 119 names have been added to the roll, but death has accounted for the loss of 49, resignation for 14 and the dues of 17 others, for reasons of illness, have been permanently remitted.

During this same period an Associate Fellowship has been established. This was created in order that full-time younger physicians might have all the advantages of the College at a reduced contribution. To date only one person has taken advantage of the opportunity, but it is hoped that, as it becomes better understood, many will do so. Also, the former policy with respect to graduates of the Hahnemann Medical School has now been changed, and already that has permitted the addition to our Fellowship of a number of excellent physicians. There remain, however, both within and outside Philadelphia, many able physicians, en-

*Read at the business meeting of the College of Physicians of Philadelphia, 8 January 1952.

tirely worthy of Fellowship, but who have not been proposed.

For admission to Fellowship the College has always required, in addition to medical competence and personal integrity, some contribution to the medical life of the community beyond the mere practice of good medicine. Consequently among its Fellows are most of the outstanding contributors to medical progress in Metropolitan Philadelphia. Such criteria must be maintained, but all of those who qualify should be admitted.

Budget

The College has continued to live within its budget, although this necessitated, during 1951, drawing on its maintenance and reserve fund for certain essential repairs to the building. For the past three years the annual income has remained practically stationary (from $84,662 to $85,951), while the expenditures have steadily increased (from $79,178 to $90,054). For 1952 the anticipated expenditures are estimated at $93,911. The net balance saved during 1949 and 1950 made possible the acceptance of the budgets for 1951 and 1952. It is obvious, therefore, that some means must be devised to increase the annual income or to reduce expenditures for future years.

As of November 10, 1951, the total estimated assets of the College amounted to $1,812,413.61. This includes the building and grounds, estimated at $887,022.28, and trust funds with a book value of $776,800.68.

The Library

In spite of the handicaps incident to inadequate space and a too frequent turn-over in the paging personnel, the latter due to substandard salaries, the library staff has continued to maintain a high grade of service to the Fellows and the medical public. For a single year the visits to the library have reached almost 16,000 and the number of books and journals supplied on request, to 67,500. Through inter-library loan and photostat services the library has made national and international contributions to medicine. Within the past year 2,342 volumes were distributed to 127 libraries in 31 of the States and Canada. Its librarians, in addition to their local activities, render national service in committee work and in the presentation of papers. The Library serves not only physicians, but also medical students, industrial researchers, historians, medical publishers, the lay press, advertising firms, non-medical faculties and students, lawyers, the clergy and social welfare groups. As stated in a recent brochure, prepared by its librarians, "It is serving a vital function in the scientific and humanistic life of the international community of medicine".

A recent study made by the library of the New York Academy of Medicine indicates that, in the areas surveyed, that library, with a budget of nearly $200,000, and the Army Medical Library, in Washington, with a budget of over $1,000,000, have approximately equal holdings. It is enlightening to learn that our library and the Boston Medical Library, with budgets equalling hardly a quarter of that of the New York library, have, respectively, in three selected subject fields, 86% and 84% of the total complete journal volumes accredited to the larger libraries.

If, however, our library is to continue to maintain its relatively important position in the country it must have a steadily increasing income. Its annual expenditures respectively for the past three years have been $39,121.90, $43,378.68 and $44,480.15. For 1952 the budget provides for $52,850. Even this amount, however, does not meet immediate needs. The salaries of the library staff, like those of the other College personnel, are still inadequate; many more books and journals should be purchased each year, and from to time, as the opportunity occurs, special works of historical value should be secured. It is for these reasons that an additional endowment of $500,000 is now being sought and that plans are underway for making an appeal to special non-medical groups for additional annual contributions.

Even with an increased income, however, the library cannot meet its steadily mounting

obligations without more stack space. Already 60,000 to 75,000 volumes are improperly housed and the stack space now available is not conditioned for the preservation of many priceless volumes. It was this situation that led President Schaeffer more than three years ago to appoint a committee to appraise the overall needs of the College and that later led to the present plans for additional building and endowment.

From time to time suggestions are made that the need for more stack space could be met by discarding much of the older, less used material, or by preserving it in microfilm form. This matter is discussed in the Annual Report on the Library and so I shall refer merely to the conclusions: 1) that discarding of the material presents difficulties of selection that would inevitably result in loss of research strength; and 2) that replacement with microfilm would be more costly, if carried to an effective length, than construction of additional stacks.

Within the past year the Library Committee, with Dr. Truman G. Schnabel as Chairman, has brought about closer relationships with the medical school libraries of the city. At a meeting of the librarians and the chairmen of the library committees of the five medical schools and of some of the larger hospitals, called by Dr. Schnabel, much interest was manifested in a program designed to render greater service to their institutions.

It is a pleasure to acknowledge the College's debt to Dr. Edward B. Krumbhaar, a former President, for his notable gift of over 200 rare historical volumes, an important addition to a field in which its Library has always been outstanding.

The Building and Development Fund

To date the Building and Development Fund, including pledges, amounts to almost $90,000. Four hundred and forty-three of the Fellows have made personal contributions, many of them representing a truly generous, even sacrificing, spirit. Other like donations are anticipated during the current year, but in the main emphasis is now being placed on the efforts of individual Fellows to secure contributions from their friends and patients. This approach has been strongly urged by a group of public spirited business men who have very kindly consented to act in the capacity of Advisers to the College. They are: Charles S. Cheston; J. Hamilton Cheston; Martin W. Clement; John A. Diemand; Albert M. Greenfield; Edward Hopkinson, Jr.; P. Blair Lee; Al Paul Lefton; A. S. W. Rosenbach; Lawrence Saunders; Geoffrey S. Smith; Leon C. Sunstein and George E. Whitwell.

Among the Advisers, Mr. M. W. Clement especially has continued his active interest and has assumed responsibility for the approach to various foundations. Already one of these has promised $250,000 if other adequate gifts can be secured. Mr. George Whitwell has been most helpful in outlining plans for the approach to public spirited citizens by the Fellows and in stimulating the group and team leaders. Mr. Al Paul Lefton has made significant contributions, both personally and through his advertising agency, by meeting with special groups, by making a member of his staff available for various purposes and by donating the preparatory work on some publicity.

It is obvious, however, that, for the accomplishment of present plans, the Fellows must exert an even more strenuous effort to elicit the financial help of their lay friends and patients. Our Advisers have set an average goal of $1,000 for the contributions to be secured through the efforts of each Fellow. Already twenty-six, through their own contributions and those secured outside the College, have met or exceeded that figure. These twenty-six have obtained a total of about $40,000. Many others will do the same. Their full effort has not yet been made.

Many Philadelphians of today, unlike those of several generations ago, are not aware of the existence and significance of this College, but as a result of the current campaign, it is becoming more widely known and appreciated. As its service to the Community becomes better understood, it is believed that $500,000 can

be obtained from the general public, and, if so, that the goal of $1,500,000 can eventually be reached. This represents a continuing challenge to the College, one that I know the incoming administration readily accepts. It cannot be attained, however, without the enthusiastic and whole-hearted support of the total Fellowship.

Meetings, Sections and Committees

The presentations made before the College at its regular Scientific Business and Section meetings during the past year have continued to be of a high order. The best attended lectures were those of Dr. A. McGehee Harvey on "Adrenal Cortical Activity and the Hypersensitive State", of Dr. James S. Simmons on "Public Health as a Weapon for National Defense", of Dr. George Thorn on "The Adrenal Cortex in Health and Disease" and of Dr. Charles C. Wolferth on "Adrenalectomy in Relation to Hypertension". At these meetings the attendance ranged from 300 to 600.

The Section on Medical History again presented its successful series of 6 lectures to the medical students of the city. In addition it had three well attended regular meetings, one in memory of a former Honorary Librarian and President of the College, Dr. Francis R. Packard. The financial support of the Philadelphia medical schools for the six lectures to students, by Drs. Shryock and Temkin, is especially appreciated and is a type of cooperation that the College welcomes from the medical schools of the city.

Mrs. Ella N. Wade, Curator of the Mütter Museum, prepared a number of articles on rare museum specimens. These were published in *Philadelphia Medicine*. The College is indebted to *Philadelphia Medicine* for these and many other valuable courtesies.

The other Sections and the various Committees of the College have performed their functions with their usual effectiveness.

Deaths

I shall now read the names of those Fellows who have died during the past year. As I do so I request that the Fellows stand.

Resident Fellows

Brooke M. Anspach
Percy L. Balentine
Joseph C. Birdsall
Carl J. Bucher
Verne G. Burden
Charles D. Hart
Harriet L. Hartley
Charles J. Hatfield
Walter E. Lee
Clifford B. Lull
John F. McCloskey
William R. Nicholson
Wilbur W. Oaks
Alexander Randall
William C. Sheehan
John A. Sweeney
Samuel M. Wilson
Oscar T. Wood

Non-Resident Fellows

George E. Price
Ralph L. Shanno

I now wish to express my thanks to all the Fellows of the College for the honor of having been its president for the three years that now come to a close. I particularly appreciate the support that I have had from all the other officers and the members of the Council and of all the committees who have unselfishly served the College with me. My thanks are also extended to Dr. McDaniel and Mr. Morse, our librarians, to Dr. Austin, our efficient executive secretary, to Miss Lang, the clerk of the College, and to the other staff members for their generous cooperation.

Finally may I congratulate Dr. Kern and Dr. Scheffey on the opportunities that await them to render service to this venerable institution.

Fellowship Contributors to the Building and Development Funds and to the Library of the College of Physicians of Philadelphia*

Names in italics indicate Fellows who have personally made or obtained from outside the Fellowship contributions of $1,000 or more

Addison, William H. F.
Adler, Francis Heed
Allbritten, Frank F., Jr.
Appleman, Leighton Francis
Aronson, Roland S.
Atlee, John L., Jr.
Austin, J. Harold

Beardsley, E. J. G.
Behrend, Moses
Biddle, Sydney Geoffrey
Blumstein, George I.
Bockus, Henry L.
Boles, Russell S.
Bortz, Edward Le Roy
Borzell, Francis Frank
Boucot, Katharine R.
Bromer, Ralph S.
Brown, Charles L.
Brown, Claude P.
Brown, Henry P.
Burnett, W. Emory

Carey, Lawrence S.
Castallo, Mario A.
Chamberlin, George W.
Chapman, John P.
Clark, John K.
Classen, Charles H.
Clerf, Louis H.
Cloud, J. Howard
Colonna, Paul C.
Cooper, David A.
Cornell, Walter S.
Corson, Edward F.
Craig, Frank A.

Dannenberg, Arthur M.
De Palma, Anthony F.
Dewees, A. Lovett
Dintenfass, Henry
Dohan, Francis Curtis
Dyer, W. Wallace

Edeiken, Joseph
Ehrich, William E.
Eliason, E. L.
Ellison, Richard T.
Ellson, J. Vernon
Ely, William C.
English, O. Spurgeon
Erb, William H.

Farr, Clifford B.
Ferguson, Lewis Kraeer
Fetter, Theodore R.
Finkelstein, Arthur
Fitz-Hugh, Thomas, Jr.
Fraley, Frederick
Friedman, Paul S.
Friedman, Reuben
Furlong, Thomas F., Jr.

Gibbon, John H., Jr.
Ginsburg, Isadore W.
Goldsmith, N. Ralph
Gopadze, Illarion I.
Grant, Francis Clark
Greene, Lloyd B.
Griffith, John Q., Jr.
Groff, Robert A.
Gwyn, Norman B.

* Resident and Non-resident, including deceased, Fellows who contributed personally or obtained contributions from outside the Fellowship, 1 February 1951–11 January 1952. Contributors up to 1 February 1951 are listed in the *Transactions & Studies* 18: 126–130, February, 1951.

Hadden, Samuel B.
Hafkenschiel, Joseph, Jr.
Hayman, Joseph M., Jr.
Herbut, Peter A.
Heyl, W. Meredith
Hitschler, William J.
Hollander, Joseph L.
Houser, Karl Musser
Hughes, P. Boland
Husik, David N.

Israel, Harold L.
Israel, S. Leon

Jacobs, Maurice
Johnson, Julian

Kaplan, Louis
Katz, G. Henry
Kauffman, M. Luther
Keiserman, Joseph
Kennedy, Patrick J.
Kern, Richard A.
Keyes, Baldwin L.
Kimbrough, Robert A.
Klauder, Joseph V.
Klopp, John W.
Koop, C. Everett
Krumbhaar, Edward B.

La Clair, Charles H., Jr.
Lamont, Austin
Lampe, William T.
Lansbury, John
Leopold, Irving H.
Lhamon, William T.
Livingood, Clarence S.
Long, Esmond R.
Lownes, John B.

McCall, Milton L.
McCarthy, Daniel J.
McClenahan, William U.
McGavic, John S.
Macfarlane, Catharine
Machella, Thomas E.
MacNeal, Perry Scott
Martin, James R.
Martin, Wm. L.
Mendell, Theodore H.
Miller, Franklin R.
Miller, T. Grier
Mohler, Roy W.
Montgomery, John B.
Montgomery, Thaddeus L.
Moore, John Royal
Muckle, Craig Wright

Naide, Meyer
Nardone, Anthony A.
Neese, Paul H.
Norris, George W.

O'Neal, Alexander Hay
Ornsteen, A. M.

Payne, Franklin L.
Pendergrass, Eugene P.
Percival, Milton Fraser
Pessel, Johannes
Pettit, Horace
Pettit, Mary DeWitt
Pfahler, George E.
Pfeiffer, Damon B.
Pfeiffer, Mildred C. J.
Piersol, George Morris

Radbill, Samuel X.
Ravdin, I. S.
Reeves, Rufus S.
Rehfuss, Martin E.
Reimann, Stanley P.
Rhoads, Jonathan E.
Richards, James L.
Rosemond, George Parrott
Rouse, George P., Jr.
Royster, Hubert A.
Rudolphy, Jay Besson
Rupp, Charles

Sampson, David Alan
Saul, Leon J.
Sayen, John J.
Scheffey, Lewis C.
Scheie, Harold G.
Schnabel, Truman G.

Schwarz, Gabriel A.
Shay, Harry
Shiffer, Paul H.
Shipman, James Shelby
Sidlick, David M.
Snodgrass, L. E.
Sommer, George N. J.
Spangler, John Luther
Stadie, William C.
Starr, Isaac
Stengel, Alfred, Jr.
Stokes, Joseph, Jr.
Strecker, Edward A.
Strumia, Max M.
Swartley, William B.

Tait, Edwin Forbes
Thorington, J. Monroe
Tocantins, Leandro Maués
Tuft, Louis

Uhle, Charles A. W.

Vander Veer, Joseph B.
Vastine, Jacob H., 2nd

Wagner, Joseph A.
Walkling, Adolph A.
Whelan, G. L.
Willard, John Harrington
Wilson, George
Wister, James W.
Wood, Dorothy D.
Wood, Francis C.
Wright, Carroll S.

Zeigerman, Joseph H.
Zulick, J. Donald

Annual Report on the Library*

Administrative

It has become popular to characterize our age as one in which the individual's knowledge is developed more intensively than extensively. Francis Bacon is said to have been the last man who commanded all the knowledge of his age. In like manner it is probably safe to claim that the generation previous to ours produced the last men who knew all that was to be known in their time of chemistry, or medicine, or many allied scientific and technical subjects. Investigators are making more detailed studies of more limited fields and are losing the ability to communicate their findings to research workers in other sciences. Hybrid disciplines such as biochemistry and biophysics, established to bridge the gaps, have merely increased the babel and have produced new specialists. Journals in the broad subject fields, such as the *Journal of the American Medical Association* and the *Journal of the American Chemical Society*, are publishing articles which fewer of their members are able to understand and much less to evaluate.

Some of the thinking men of our generation believe that the fate of the major research library as anything more than a depository of knowledge hangs in the balance. They fear the tide of publication is swelling so rapidly that the scientist of the future who searches the literature will not have time for original research. They plead for strengthening the powers of observation through experience even at the possible expense of being unaware of the latest therapeutic measures. This is a message of despair to the librarian who expects his library to be an effective weapon in man's war against disease and ignorance. When scientists are no longer able to profit by the sharing of their experiences, scientific advance will have been cut off by a paper curtain as effective as the strictest censorship.

Our own library apprehensively views statistics which show the third year of declining numbers of visitors to the library and of volumes consulted in the library. The fact that the number of volumes withdrawn from the library has risen against this trend is partly caused by a growing inter-library loan trade which may prove that our readers feel obliged to stay closer to their laboratories. This decline was originally attributed to the initiation of the contribution plan in July 1948 but it now seems clear that other factors are involved. Our public library colleagues are attributing similar trends to the advent of television but our more scientifically minded library committee members have suggested other influences which may be significant.

The increased popularity of post-graduate seminars which serve as refresher courses in fields of specialization indicates that some physicians are electing this method of keeping abreast of current developments rather than attempting a personal review of the literature. Further assistance to the busy practitioner has been provided by capsule summaries distributed by the pharmaceutical houses. Library committee members also note a growing interchange of reprints among the men in the subject specialties and agree that the public's greater demand for medical services has reduced the free time of the practicing physician. A shift in medical school emphasis to the laboratory has further reduced undergraduate time available for independent study. Locally the picture has been affected by recent extensions of library hours by most of the neighboring medical schools coincident with the improvement of their services and facilities. We have also witnessed the recent establishment of new private and governmental libraries in the biological sciences catering to highly specialized clienteles.

The important thing is not to determine the cause of the trend or even to prove that such a trend exists but it is rather to plan the role

* 1 November 1950–31 October 1951.

which the research library can play under changing conditions. Should we abandon research libraries in favor of robot-minded machines into which clerical workers can feed coded facts to be regurgitated upon demand? Shall we consign the knowledge of the past to the pulp mill admitting that it is no longer possible to profit by its lessons? Shall we cut off man's access to scientific facts except by tedious laboratory research on problems which may have previously been solved?

The solution may lie in the realms of the electronic library but we prefer to trust that it is to be found in stressing the fundamentals of good library service. These fundamentals include proper publicizing of the library's facilities to its present and potential users; well-informed selection of the most significant publications; intelligent and courteous service to our telephone clientele and to the reader who comes to the library, including instruction in the use of the library's tools; diligence and imagination in the preparation of those tools to insure their usability; good housekeeping practices which will speed our services and control their costs; exertion of our influence in the bibliographical world for the production of comprehensive indexes and abstracts speedily prepared and well arranged for the convenience of the busy research worker. In these ways we believe the modern research library will be able to expedite the research worker's struggle with the increasing flood of literature. Medical research is entitled to expect the library to be as efficient and as well-appointed as the laboratory and can reasonably expect a good return for time properly spent in either.

The translation of these broad objectives into practical measures reduces our discussion to one of homely administrative procedures.

Publicity, or more properly public relations, has included the distribution of a poster, a leaflet, and the regular booklists, and the presentation of a lecture and library tour for the Freshman class of the Woman's Medical College and the Training Class of the Free Library of Philadelphia. The library's "Selective list of reference sources" was revised and distributed to the former group. The library prepared exhibits for each of the six weekly lectures in the course on medical history arranged for the medical students in the area by the College Section on Medical History. Catalogues of the exhibits were provided as usual. The library participated in the College's indoctrination of its new Fellows by conducting them through the library's rooms and discussing the library's resources and services. A conference of library committee chairmen and librarians of the local medical schools was invited to meet with the library committee and the administrative staffs of the College and the library to discuss possible ways for the College library to increase its usefulness and to provide a forum for the consideration of mutual problems. The letters which are appended to this report were received after the meeting and indicate the appreciation of these schools for the assistance which we are able to give at the present time, but we suspect that the fullest possibilities of these relationships have not been explored and we shall continue our efforts to extend the library's services in this direction.

Public relations aspirations as yet unattained include the desire to know more intimately the ramifications of medical research in this area. A closer contact with actual research projects and with their personnel would indicate our interest in the practical aspects of research and might suggest new lines of service for the library. Fellow librarians who read this report will sympathize with our complaint that internal affairs demand so much attention that there is little opportunity for the realization of these ambassadorial ambitions.

Book Selection continues to be based on methodical combing of announcements, book reviews, and booklists. Sporadic attempts are made to solicit the aid of our readers in their chosen fields. Orders are almost always entered for books which we have been unable to supply upon demand. A wary eye is kept on the allied sciences and on general bibliography for books whose approach, implications, or factual content will augment our collection or inter-relate medicine to science and social science. We

recognize that considerable delays often occur after publication before some significant books are delivered to our readers and we hope to regulate this matter.

Readers' Service is the area within which libraries make their most lasting impressions. Reading rooms which would be adequately manned for periods of peak demand would be overstaffed during slack hours. Previous reports have recommended the employment of an assistant at large for reading room duty with responsibilities in other phases of the library program as pressure permits. Such an assistant could instruct our readers in the use of the library as an efficient instrument. Access to the increasing volume of literature has been speeded by the creation of new printed guides and home-made indexes. It is not surprising that readers who are unaware of their existence show an increasing reluctance to find their own answers. The reader who expects to be spoon fed information might be converted into an intelligent and willing library user by sympathetic instruction centered around his actual problem. This closer observation of readers' interests and habits would suggest the creation of new bibliographical aids and the possible redesigning of old ones.

Instruction in the use of the library and the maintenance of library tools should exploit methods of research common to widely variant fields. Although the new sciences which are being born are matching strides in growth with the older ones, there are certain patterns of knowledge which are universal and bibliographical methods once thoroughly learned can be employed in many different subject fields. The perfection of these methods and their adaptation to the practical concerns of our readers are part of our mission. When the literature has become so voluminous that we cease to have first hand knowledge, the proper application of bibliographical methodology will supply it.

Methods. Librarians must continue to create catalogs and routines which can be mastered by the average reader. They must exert their influence for better and more comprehensive indexing and abstracting services which will appear promptly enough to be of real value. Activities of members of our own staff in this area are indicated in another part of this report. Librarians must maintain orderly stacks to insure the rapid location of material. They must practice all possible operating economies to keep the cost of research within reasonable limits. They must provide sufficient recognition, both economic and professional, for their personnel to maintain high morale and inspire their best efforts. In short, the challenge of our times can only be met if we keep our perspectives broad without losing sight of the mundane details which contribute to the smooth operation of the modern research library.

Microcopy and the Library. For reasons noted below special consideration is being given here to the possible use of microcopy as a solution to the problem of providing space for the rapid servicing and safe preservation of our book collection.

Man's impatience with peaceful evolution leads him to try to apply each new invention or cure to every problem or ill. The invention of microfilm and other forms of microcopy was first heralded as the librarian's answer to the ever-growing flood of literature and as a possible alternative to orthodox stack book storage. Microcopy and the other manifestations of the science of cybernetics have advanced their frontiers until their limitations as well as their potentialities are now more clearly realized.

Since the College is engaged in a vigorous campaign for more funds for the library and since overcrowded bookstacks is one of our greatest problems, it is appropriate to examine the possibility of using microcopy as an alternative to building new stacks. This examination has led to a consideration of the following factors.

An examination of the financial factor shows that in the College's case the erection of new stacks would be less expensive than filming the equivalent number of books. Fortunately the College owns unused land immediately adjacent to the present stack which would serve admirably for an extension. Present estimates call for the construction of a stack providing

for 160,000 volumes at a cost of $438,000, or $2.72 per volume. The cost of filming existing volumes would be about $15.00 per volume. The same conclusion can be reached by a linear foot comparison. New stack storage space would cost about $19.04 per foot. This foot of shelf holds about 4,000 pages, the filming of which would cost about $120.00.

Then, it must be recognized that the selection of older volumes for microfilming would require a volume by volume examination of the present collection by experts in each of the subject fields. Subsequent to the photographing, the films must be accessioned, the filmed volumes dispersed with regard for their potential usefulness elsewhere, catalogue records must be changed, and the remaining volumes reshelved to utilize the space thus provided. This program would require special personnel under professional supervision above and beyond what the present library staff could provide.

Once this material has been filmed, its use outside of the library will be restricted to those patrons who own or have access to a reading machine. Its use within the library will be more time consuming than the use of the original material. The same length of time is required to deliver a volume or its microcopy to the reader but in the case of the microcopy, it is necessary to put the reading machine into operation, remove the film from its carton, thread the film on the machine, scan the film for the desired reference, and to unwind the film to prepare the machine for the next film, whereas the original volume need only be opened to the proper page. Also, it is difficult to make textual comparisons without multiple reading machines or extensive note taking.

The library as a potential supplier of microcopy faces other problems. It would be required to operate or have convenient access to a photographic laboratory. The making and distribution of microcopies without specific permission of the copyright owner is done in a legalistic twilight zone unconfirmed by judicial opinion and vulnerable to such a decision when the practice becomes widespread enough to be economically significant.

At the current publication level the library, as a potential user of microcopy, finds the immediate supply and foreseeable prospects too limited to serve as justification for the abandonment of the plea for more stack space. Only 106 medical journals were available on a microfilm subscription basis in July 1950, so it will be a long time before this alternative, whose acceptability remains questionable on other grounds, can be thought of as providing a possibly significant answer to the library's list of over 1,500 journals currently received.

The day of the electronic library may be closer than we imagine. Facsimile transmission by television and automatically reproduced punch card bibliographies may, and probably will, become common library realities within the next generation; but until they and other devices, such as microcopy, have further proved their value and adaptability to a research library with our particular obligations, it would be folly to deny our responsibility to house our present collections adequately and to provide for reasonable growth. We are inclined to think, putting it in homely terms, that the library runs less risk of losing its pants if it keeps its shirt on.

Benefactors. Without pretending to offer a complete list of those persons whose gifts have materially aided the library, the administration wishes to insert its grateful acknowledgement in this report for the grants of $1,000 each from Sharp and Dohme and from Wyeth Inc. A donation of $750 was received from Smith, Kline and French and $500 from the National Drug Company. Among the Fellows, Dr. J. Monroe Thorington continued to make substantial donations for rare book purchases.

E. H. M.

Historical

Acquisitions.

The "news" of the year in this department, hinted at in our last preceding report, was receipt of over 200 volumes of *rariora* from the

private collection of our incomparable friend and former president, Dr. Edward B. Krumbhaar—a donation which is to be followed by similar, though not so extensive, ones in succeeding years.

The immediate fact to be noted in connection with this wonderful gift is that each of the items represents a positive addition to our resources: the catalogue of Dr. Krumbhaar's library had been checked against ours a year or so previously, with the result that duplications were eliminated in advance.

As Dr. Krumbhaar is by avocation an historian, like his older ex-presidential colleague the late Dr. Packard, whose library came to us last year, his interests have been somewhat broader than those of the purely specialist collector, though his vocational concern with pathology is clearly marked out by the number of important texts in that field. It is unfortunately impossible, within the limits of this report, to explore the fascinating variety of the collection. Mimeographed catalogues of an exhibit of some 60 of the items are available, but obviously give only an imperfect idea of how much richer the library now is.

Receipt of these two important libraries—the Packard and the Krumbhaar—within two years creates an even more imperative need, however, for that expansion of quarters and staff towards which the College administration is valiantly bending all its efforts. With stacks desperately overcrowded, with cataloguing staff overworked and unable to give time to the specialized demands of cataloguing *rariora*, these mines remain perforce largely unworked. The College administration and many of the other Fellows continue to demonstrate a keen and generous understanding of the essential role the historical collections play in the services demanded of a research library such as ours. Together, we must continue to press home the point that the library administration is powerless to capitalize on these riches already in its hands until adequate housing and staff are provided. A Rare-Book Room of sizeable dimensions is, far from being a luxury, quite as essential now to the library's proper functioning as any other of the service rooms. We shall continue to acquire whenever, wherever, and however we can every possible historical item germane to our field; but we must continue to emphasize that this is mere hoarding at the present time, that what is most needed is the wherewithal to construct a suitable addition to a handsome, well-beloved building that will provide adequate quarters for one of the most outstanding collections of materials for medico-historical research of which our country can boast. And it may be suggested here that these quarters should provide alcoves which could be dedicated to distinguished special collections such as those under review. When a man has spent his life bringing together a useful library of historical texts, it is reasonable that he should wish to have it preserved in a way calculated to perpetuate the memory of his devotion and generosity. The library would be serving its own interests, we believe, if it could offer such sanctuary to private collections that would add notable value to its resources.

Some other historical acquisitions of special interest are noted as follows:

16th Century

Codronchius, Baptista (1547–1628). De vitiis vocis, libri duo. Frankfurt, heredes Andreae Wecheli, 1597. Gift of the *College's Section on Otolaryngology.*

Codronchi, not a new name to our catalogue, was a one-time famous Italian physician whose published works range through several fields; in each he is said to have made contributions that were original and, in some cases, fundamental. This work, *De vitiis vocis*, is regarded as the first monograph on diseases of the vocal apparatus. The first part deals with the anatomy and physiology of the larynx; the second, with its diseases and methods of treating them. The text is described as showing sound medical practice and a reawakening spirit of observation. This first edition contains also two other works by Codronchi, including a noted one on legal medicine, which we also had not previously owned.

Diaz, Francisco (fl. ca. 1580). Tratado

nuevamente impresso, de todas las enfermedades de los riñones, vexiga, y carnosidades de la verga, y urina. Madrid, Sanchez, 1588. *Gift of J. Monroe Thorington, M.D.*

Diaz' *Tratado* (of which this is the first edition) ranks as the first printed treatise on diseases of the kidney, bladder, and urethra; and the author, physician to Philip II, is consequently regarded as the founder of urology. Doubtless contributing in part to the book's great rarity is the fact that it contained sonnets in praise of the author's surgical skill by the celebrated Cervantes and Lope de Vega. Unfortunately, the leaf containing the Cervantes sonnet is missing in our copy. The section on the bladder contains illustrations of surgical instruments.

17th Century

DI CAPOA, LIONARDO (1617–95). Parere . . . divisato in otto ragionamenti, ne' quali partitamente narrandosi l'origine, e 'l progresso della medicina, chiaramente l'incertezza della medesima si fa manifesta. 3. imp. Naples, Raillard, 1695. *Purchased by the library.*

The "incertitude" of medicine—i.e., the impossibility of reducing it to the relative fundamental stability of exact science—has distressed the uncompromisingly scientific mind for many centuries. The Neapolitan Capoa, student, successively, of theology, law, and medicine, was one of these. He founded a society, called the Academy of Investigators, whose aim was to make new researches in medicine. But his skepticism, chiefly in regard to the art of healing, was carried to such extreme lengths that he made many enemies among his confreres. In this book—the *Parere* (Opinions) of Capoa—history is used for the avowed purpose of attacking medicine as an inconclusive and conjectural science. In the second part of the work (which carries a separate title-page but with the same imprint as that of the first part), Capoa sets out to prove that we do not know the properties of medicaments, that one cannot count on their actions, and that, furthermore, we have no precise knowledge of their manner of working. The irritation which such a nihilistic attitude might create in any age is understandable; what would be enlightening is to know how far Capoa's 17th century master chamber of incertitudes has been reduced by the development of biochemistry, psychiatry, and pharmacology in the intervening two and a half centuries to confines equally challenging but less intimidating; since we now know, more than ever before, that creative man, though he sometimes moves slowly, is dedicated to, and is not to be put off from, resolving the incertitudes that separate him from perfect adaptation to his environment.

18th Century

ADAMS, GEORGE (d. 1773). Micrographia illustrata, or, The knowledge of the microscope explain'd. 2d ed. London, the author, 1747. *Gift of George W. Norris, M.D.*

The *Micrographia* of George Adams ("Mathematical, Philosophical, and Optical Instrument-Maker" to George III) contains "a Description of the Nature, Uses, and Magnifying Powers of Microscopes in general." One of the sections, "Of the Circulation of the Blood, and how to examine it by the Microscope," draws heavily on Leeuwenhoek's letters to the Royal Society and is of particular interest for its demonstration of the common knowledge of hematology in the age of Haller. This copy had been, since 1789, in a family (Norris) whose contributions to Philadelphia medicine and the College have been as distinguished as they are well-known.

RAULIN, JOSEPH (1708–84). Abhandlung von der Lungensucht, nebst ihrer auf Wahrnehmungen gegründeten Verwahrungs—und Heilungsmethode, mit Anmerkungen und Vorrede von Benedict Christian Vogel; übersetzt von J. G. Grundmann. Jena, 1784. *Gift of (the late) Frederic H. Lewey, M.D.*

Raulin's treatise on pulmonary phthisis (said to contain some excellent observations) brings us, though in German translation, a text by a French royal physician and prolific writer, several of whose other works are in the library, though one or two of them, again, in German translation.

TARIN, PIERRE (1725–61). Dictionaire anatomique suivi d'une bibliothèque anatomique et physiologique. Paris, 1753. *Purchased by the library.*

Pierre Tarin's dictionary of anatomy, and bibliography of anatomy and physiology, is to be understood as a glossary and bibliography applicable to his highly regarded article on anatomy in Diderot's famous *Encyclopédie.* He acknowledges having drawn upon Haller's "treatises on the animal economy" (the work is said by others to derive from Haller's *Methodus studii medici*), but of course he did not have the advantage of Haller's great *Bibliotheca anatomica,* which was not published until over two decades later.

19th Century

ALIBERT, J. L. (1768–1837). Éloges historiques composés pour la Société médicale de Paris, suivis d'un Discours sur les rapports de la médecine avec les sciences physiques et

morales. Paris, 1806. *Gift of E. B. Krumbhaar, M.D*

Nowhere but in France of the 18th century, possibly, would one find a celebrated dermatologist (Alibert) composing extended memoirs for a local medical society on two foreign physiologists (Spallanzani and Galvani) and a truant from medicine (Pierre Roussel) whose most notable production (a profoundly influential one) was a work entitled, *Système physique et moral de la femme.* An addition of equal if not greater value to our resources is the concluding discourse on the relations between medicine and the physical and moral sciences, since Alibert had a vast fund of erudition, wit, and feeling to draw upon.

FORBES, JOHN (1787–1861). A manual of select medical bibliography, in which the books are arranged chronologically according to the subjects. London, 1835. *Gift of the Mercantile Library, Philadelphia.*

Fulton has recently described John Forbes' medical bibliography as "the first serious attempt on the part of anyone in the English-speaking world to give a subject classification for medical literature." Our collection of historical medical bibliographies is obviously significantly enriched by our friendly neighbor's gift of this classic.

MCCAMANT, JOHN (1787–1862). Manuscript receipt book. *Gift of Martin L. Andes through Mrs. Alfred J. Ostheimer, 3d.*

A record of the medical career of Dr. McCamant is not easily come by, but he is said to have been at one time physician to his fellow Pennsylvanian President James Buchanan, and to have been, himself, in his later years, Speaker of the House, at Harrisburg.

RAUSSE, J. H. Ueber die gewöhnlichsten ärztlichen Missgriffe beim Gebrauch des Wassers als Heilmittel. Zeitz, 1847. *Gift of (the late) Frederic H. Lewey, M.D.*

Rausse's works on hydropathy, translated into Swedish and English (the library has his "The water cure applied to every known disease"), and doubtless other languages, reflect the widespread interest in the subject in the 19th century. Like Priessnitz, the most famous popularizer of "water-cure", whom he attacks in the first of these two books, Rausse represents, however, the cult, and not the scientific, interest in the subject.

Exhibits. Reference has already been made to a catalogued exhibit of some 60 of the rare volumes from the Krumbhaar donation. Another major exhibit that excited unusual attention was that of over 100 medical bookplates from the collection, numbering between four and five thousand, of our Fellow Dr. Samuel X Radbill. This exhibit was prepared in honor of the 75th anniversary of the founding, in this city, of the American Library Association. Again, catalogues were made available to visitors. As usual, the library supplied pertinent exhibits for each of the six lectures on medical history offered the medical students of the city by our Section on Medical History with the coöperation of the medical schools, and annotated lists of the books displayed were provided.

Authors' Acknowledgements. Two distinguished historical works published during the year contain more than perfunctory acknowledgement of the authors' debts to our historical collections: L. H. Butterfield's 2-volume *Letters of Benjamin Rush;* and Dean P. Lockwood's *Ugo Benzi.* The library's very rare 16th century pictorial German broadside announcing the birth of quintuplets was reproduced in an English publication, Harvey Graham's *Eternal Eve,* along with a translation of the text published by the library some years ago. W. R. Le Fanu's *Bio-bibliography of Edward Jenner* disclosed the information that the library has the second largest collection of Jenner letters in this country, and the fourth largest in the 70-odd European and American collections circularized by the author.

Publications and Other Activities. The following publications by the librarian drew upon the library's historical resources:

Historical source material of all classes in all types of medical libraries, *Bull. M. Lib. A.* 39: 9–11, 1951. (Read at the 49th Annual Meeting, Medical Library Association, Boston, 20 June 1950.)

Book review: Earnest, E. S. S. Weir Mitchell: novelist and physician. Phila., 1950. *Ibid.*, pp. 63–4.

Francis R. Packard and his role in medical historiography. *Bull. Hist. Med.* 25: 66–85, 1951.

Proceedings of the Section on Medical History devoted to the late Francis R. Packard and the 200th anniversary of the Pennsylvania Hospital. Remarks, *Trans. & Stud. Coll. Phys. Phila.* 4th ser. 19: 83–4, 1951.

The following papers were read but have not been published:

Guy de Chauliac's 14th century history of surgery. (Read before the Johns Hopkins Medical History Club, 5 March 1951. Part of a larger study being prepared for publication.)

The beginnings of American medical historiography. (Read at the Annual Meeting of the American Association of the History of Medicine, 3 May 1951. To be published in the *Bulletin of the History of Medicine.*)

Above all else, this section of the report should pay tribute to the officers and many other Fellows of the College whose stimulating interest and practical support will eventually bring about the establishment of that well-housed and well-organized historical department that the times and the College's great heritage call for.

W. B. McD., 2D

The Staff

The library was represented by Mr. Morse at the 50th meeting of the Medical Library Association, held in Denver, in June. The Association appointed the following staff members to its committees: Mrs. Bready was reappointed to the Committee on Periodical and Serial Publications. Mr. McDaniel was reappointed to the Committee on Abstracting and Indexing. Mr. Morse was appointed to the Committee on Gifts and Grants.

Mrs. Maines was chairman of the Hospitality Committee of the Social Science Group of the Special Libraries Council of Philadelphia and she has been appointed to the Membership Committee of the newly formed local chapter of the Medical Library Association.

Miss Hodge served as Secretary of the Social Science Group of the Special Libraries Council of Philadelphia and was a member of the Publicity Committee of the Council.

Mr. Morse served as Managing Editor of the *Bulletin of the Special Libraries Council* and as Advertising Editor for the new 8th edition of the *Directory of Libraries and Information Sources in the Philadelphia Area.* He was elected vice-chairman of the local chapter of the Medical Library Association. He is serving as vice-president of the board of trustees of the Narberth Public Library. He participated in a panel discussion of the "Ratio of Library Service to the Inflated Dollar", under the auspices of the Pennsylvania Library Association.

Mr. McDaniel attended the annual meeting of the Association of Honorary Consultants to the Army Medical Library, held in Washington. A note on his historical activities appears in the historical section.

There was a large turnover in the paging staff during the year and a complete change in the cataloguing personnel. Miss Muriel Hodge, former Cataloguer of the Lippincott Library at the University of Pennsylvania, was appointed to the position of Cataloguer. Miss Lillian Ceci was promoted from the position of Page to that of Assistant Cataloguer.

The administrative assistant librarian and the librarian are particularly grateful for the splendid spirit of cooperation shown by the staff throughout the year. In view of the large number of personnel changes it is especially to their credit that all schedules were maintained and that the flow of work was uninterrupted.

The staff roster, as this report goes to press, follows:

Librarian
W. B. McDaniel, 2d

Administrative Assistant Librarian
Elliott H. Morse

Head Cataloguer
Miss H. Muriel Hodge

Assistant in Charge of the Reading Room
Mrs. Maud G. Maines

Assistant in Charge of the Periodicals Room
Mrs. Elizabeth F. Bready

Assistant Cataloguer
Miss Lillian Ceci

Secretary to the Librarians and General Assistant
Miss Kathryn E. Haegele

Photostat Operator and Page
Miss Margaret Greene

Pages
Miss Patricia Alexander
Miss Blanche Perrin

Statistical Summary

INVENTORY

	1951	1950
Total number of accessioned[1] items	179,566	173,450

	1951	1950
Incunabula	416	416
Manuscripts (including a few typescripts)	779	741
General	174,355	172,293
Accessioned pamphlets	4,016	
	179,566	173,450

Total number of unaccessioned[1] items	322,445	325,446
Reports	26,916	26,875
Periodicals "reserve"[2]	8,526	8,186
Theses and Dissertations	55,828	55,177
Pamphlets and reprints	231,175	235,208
	322,445	325,446
Total number of current periodical publications regularly received	1,603	1,477
Portraits[3]	78,590	76,617

Distribution of This Material

	Accessioned Items	Unaccessioned Items
General Library (including the Lewis Library)	175,239	322,441
On permanent deposit:		
Gross Library	3,910	4
Parry Library of the Obstetrical Society of Philadelphia	217	0
Mütter Museum[4]	200	0
	179,566	322,445

Current Periodicals

	Purchased	Exchange or Gratis	Total
U.S.A.	273	384	657
Western European Continent	523	46	569
Latin America and West Indies	34	94	128
United Kingdom and Eire	111	32	143
Canada	5	23	28
Eastern European Continent	4	3	7
Asia	26	19	45
Africa	3	5	8
Pacific	4	14	18
Grand Total: 1951	983	620	1,603
Grand Total: 1950	949	528	1,477

[1] Accessioned items in this library comprise the total number of bound volumes and such unbound pamphlets as have been catalogued as separate bibliographical units regardless of their size.

This year's report notes the transfer from the unaccessioned to the accessioned category of 4,016 pamphlets of 'volume' importance which have been separately accessioned and catalogued under a program instituted some years ago. There remain many thousands of similar items awaiting accessioning and cataloguing. A true quantitative and qualitative picture of the library's holdings cannot be presented until this wealth of neglected material has been processed and duly registered in our 'accessioned', or 'volume', count.

[2] More-or-less complete duplicate volumes of periodicals.

[3] Including 118 oil, and 422 other, framed portraits in the care of the Committee on College Collections. The count of portraits represents the number of entries on the cards in the portrait catalogue. The entries represent, in turn, both loose portraits and those in books, many of them, of course, being merely different reproductions of a single original.

[4] The books of the Mütter Museum are not permitted to be removed from the College building.

New titles: A total of 63 periodicals was added in 1950–51. Thirty-five of these were purchased; 28 received in exchange or gratis. Forty-six began with volume 1. The remainder of the increment in the grand total represents variations in publication schedules and reestablishment of exchange and gift lists as the result of an active claiming program.

Separate Issues received, checked-in on the cards, and shelved totaled 14,972. In addition, thousands of duplicate issues were received, as usual; 340 of these were retained for our 'reserve' files, no attempt being made to count those held merely for exchange or other use.

Visitors to the Norris Room for the year totaled 4,612.

Readers' Use of the Library

Library Hours. The library was open, during the academic year, from 9:30 to 9:30 on Mondays and Wednesdays; from 9:30 to 5:30 on the other weekdays. During the latter half of June, in July, August, and the first half of September the library was open from 1 to 9:30 on Tuesdays; from 9 to 5 on the other weekdays, except Saturdays, when it was closed. The following legal holidays were observed: Thanksgiving (beginning at 5:30 on the preceding evening), Christmas and New Year's (and the day preceding each), Memorial, Independence, and Labor Days.

Number of visitors:

	1951	1950	Totals 1951	Totals 1950
Days (including evenings)	(294)	(289)	8,708	10,145

Circulation of books:

Number of volumes taken out (Books: 2,266; Periodicals: 5,223)	7,489	7,172
Number of volumes consulted in the library[5]	54,447	57,294

Inter-library loans: The library sent 2,342 (1950: 1,754) volumes on inter-library loan to 127 libraries in 31 (1950: 21) States and Canada and has borrowed 32 (1950: 19) volumes from 3 (1950: 1) libraries.

Photostats: 2,142 photostatic prints were furnished on request (1950: 3,196).

Acquisitions and Accessions

Accessioned Acquisitions:

1951: 2,100 volumes (1,492 by purchase; 471 by gift; 137 by exchange). (*Books:* 725; *Periodicals:* 1,375); 133 pamphlets.

1950: 2,175 volumes (1,452 by purchase; 551 by gift; 172 by exchange). (*Books:* 740; *Periodicals:* 1,435).

Non-accessioned Acquisitions[6]*:*

1951: 41 Reports (1950: 51).
651 Theses (1950: 1,587).
135 Miscellaneous items (1950: 383)

Donations

The donors for the past year number 205 (1950: 241). The library is indebted for large gifts of books, pamphlets, and unbound periodicals to the following donors: Drs. A. J. Bedell, S. Bellet, K. Chouké, R. A. Kern, E. B. Krumbhaar; Boston Medical Library; Jefferson Medical School Library; Lea & Febiger; Smith, Kline & French Laboratories; South African Institute for Medical Research; Woman's Medical College Library; Wyeth, Inc.

Various publishing houses have presented volumes as follows: Blakiston Co., 18; F. A. Davis Co., 1; Lea & Febiger, 18; J. B. Lippincott Co., 14; W. B. Saunders Co., 45.

Other individual donors were as follows: Dr. H. Beerman; Prof. W. J. Bell, Jr.; Drs. W. N. Bradley, R. W. Brust; L. H. Butterfield; Dr. M. A. Castallo; Mr. D. L. Cowen; Drs. D. M. Davis, F. B. Faust, E. C. Faust; J. E. Flynn; Drs. F. Fraley, J. F. Freeman, R. Friedman, J. S. Hepburn, E. Hess, L. A. Hopkins; an Italian Friend (through Mr. J. Liguori); Drs. C. Jackson, C. L. Jackson, J. V. Klauder, W. E. Krewson, 3rd, W. G. Lennox, F. H. Lewey; Prof. D. P. Lockwood; Drs. F. D. W. Lukens, D. Macfarlan, T. H. McGavack, F. M. McPhedran, P. J. Mandabach; Mr. E. S. Morris; Drs. C. W. Muckle, S. Mudd; Miss A. Nock; Drs. G. W. Norris, J. Ono, H. W. Orr, L. A. Peer, H. Pettit, G. E. Pfahler, S. X Radbill, H. S. Read, J. V. Ricci, M. P. Rucker; Prof. K. F. Russell; Drs. C. Stamm, R. M. Stecher, N. Steinberg; Temple

[5] The number of volumes "consulted in the library" includes only those supplied on demand. Readers have access to the bound volumes of periodicals and reference works kept on the shelves in the Reading Room; the Fellows, and occasionally others, by special permission, have access to the book-stacks. There are, therefore, many volumes consulted of which no accurate record can be kept.

[6] As usual, not all the pamphlets, theses, and numbers of various journals listed as received had been checked for keeping or discard at the close of the library year.

University Medical School Library; Drs. J. M. Thorington, L. M. Tocantins, P. Williams, I. J. Wolman, A. C. Wood, T. K. Wood, W. Zentmayer.

Exchanges

The *Transactions & Studies* was sent, either in exchange or as gift, to 238 organizations.

The library received a number of journal issues through the Medical Library Association Exchange and supplied duplicate journals to other libraries through MLA, UNESCO, and others.

Theses and dissertations to the number of 651 have been received on exchange from the following European schools of medicine: Universities of Amsterdam, Basel, Berlin, Bern, Copenhagen, Erlangen, Geneva, Göttingen, Heidelberg, Jena, Lausanne, Leiden, Louvain, Lund, Uppsala, Utrecht.

Work of the Cataloguers

	1951	1950
Accessioned items catalogued or recatalogued	670	767
Unaccessioned items and Fellows' reprints catalogued by author or by author and subject	209	156

Approved:
Truman G. Schnabel
Chairman

W. B. McDaniel, 2d
Librarian
Elliott H. Morse
Administrative Assistant Librarian

APPENDIX

Letters received by Dr. T. Grier Miller, President of the College, expressing appreciation of the Library's services to the medical schools of Philadelphia.

HAHNEMANN MEDICAL COLLEGE

Dear Doctor Miller:

On behalf of the faculty and students of Hahnemann Medical College, we wish to thank the College of Physicians for their assistance to us. We depend upon your large library to supplement the resources of our own collection and frequently borrow material from you which would not otherwise be available locally. This inter-library loan is just one of your services which greatly aid and expand the field of research in medical and scientific literature in this city.

Your library staff has been most generous about helping us in every possible way. We are grateful to them and to the College of Physicians for the spirit of mutual understanding and cooperation which exists here.

Very sincerely yours,
Lucy Finkel
Librarian
Charles L. Brown, M.D.
October 12, 1951 *Dean*

JEFFERSON MEDICAL COLLEGE

Dear Doctor Miller:

The Students, Faculty and our own Library have made, in the past, frequent use of the unexcelled facilities of the Library and the treasures of the College of Physicians of Philadelphia. In this and other respects, the College of Physicians lends important support to the activities in the field of medical education and research in Philadelphia.

Sincerely yours,
George A. Bennett, M.D.
October 10, 1951 *Dean*

TEMPLE UNIVERSITY SCHOOL OF MEDICINE

Dear Dr. Miller:

The Library of the College of Physicians has been of great assistance to the Faculty and Students of Temple University School of Medicine. This aid has been manifested in many ways. Although many of the Faculty are members of the College, all have been welcomed and assisted in every way. Students have easy access to the valuable stacks and files. Not the least of the great services of the College is its willingness to furnish us with journals on interlibrary loan when they are not available in our own institution. I am sure the College library influences our whole medical community in a favorable way.

Sincerely yours,
William N. Parkinson, M.D.
October 31, 1951 *Dean*

UNIVERSITY OF PENNSYLVANIA, SCHOOL OF MEDICINE

Dear Dr. Miller:

Dr. Mitchell has sent me a copy of his letter to you of October 17.

I want you to know how deeply we appreciate the action taken by the College of Physicians which makes it possible for students in the School of Medicine to utilize the great Library of the College of Physicians.

Many, many thanks.

Sincerely yours,
I. S. Ravdin, M.D.
Vice President in Charge
October 23, 1951 *of Medical Affairs*

UNIVERSITY OF PENNSYLVANIA, SCHOOL OF MEDICINE

Dear Dr. Miller:

I should like to express to you personally and on behalf of the University our deep appreciation for the past and present courtesies which have been extended to students in the School of Medicine by the College of Physicians.

The availability of the College library is a great boon, both to faculty and students, offering them facilities which it would not be possible to replace. I trust that you will extend to the proper authorities of the College this acknowledgment of our debt to you.

Sincerely yours,
JOHN McK. MITCHELL, M.D.
Dean

October 17, 1951

WOMAN'S MEDICAL COLLEGE OF PENNSYLVANIA

Dear Dr. Miller:

I want you to know that the faculty, staff and students of the Woman's Medical College consider that the library of the College of Physicians of Philadelphia renders an outstanding service. They gain greatly from the reference books, rare periodicals and meetings that are not available to them through any other institution.

This is just a word of support for you and other members of the College who are actively engaged in the development of the library.

Very sincerely yours,
BURGESS GORDON, M.D.,
President

November 7, 1951

Annual Report of the Committees on the Mütter Museum and College Collections

The Museum

The Mütter Museum was open to Fellows of the College, physicians, students and the general public from 10:00 to 1:00 and from 2:00 to 5:00, except Saturdays, when it was open from 9:30 to 1:00. On evenings of the Stated Meetings of the College it was open until 8:30 P.M.

Besides individuals from all parts of the country, groups of student nurses from various hospitals, classes from the Free Library, Woman's Medical College, Gillespie High School and the Junto Evening School visited the Museum during the year. These numbered 1221.

The usual arthritis specimens were used to illustrate a lecture on the subject of arthritis, held at the College.

To further publicize the museum, short articles on museum and College specimens have been written and appear occasionally in *Philadelphia Medicine.*

Two special exhibits, one of 18th century medicine cases, and another of 19th century hypodermic needles and clinical thermometers, were prepared in conjunction with the Section on Medical History's lectures on the history of medicine for medical students.

The Section on Otolaryngology used the Hyrtl Collection of ossicles and labyrinths of the ear of all mammalian families, and the Adam Politzer Collection of tympanic membranes for demonstration in connection with a special meeting held in November.

Mrs. Ella N. Wade was reappointed curator and clerk-technician for the year 1950–1951.

Accessions to the permanent collection of the Mütter Museum for the year, and falling under the provisions of the Mütter Deed of Gift, are as follows:

Presented by Mrs. Horace J. Williams:

Monochord devised by Dr. H. J. L. Struyken of Breda, Holland and augmented by Prof. Karl Schaefer of Berlin, formerly belonging to Dr. Horace J. Williams.

Model 2-A Audiometer (1922)

Presented by Dr. William Zentmayer:

Metal stethoscope formerly belonging to Dr. Zentmayer's brother, Dr. Louis Zentmayer, date 1879.

Pocket case formerly belonging to Dr. Louis Zentmayer.

Loring ophthalmoscope

Fox's ophthalmoscope given to Dr. Zentmayer by Dr. Burton Chance.

Loring ophthalmoscope formerly belonging to Dr. William F. Norris.

Stokes' rotary prism

Presented by Kenneth K. Kline, D.D.S.

Obstetrical forceps

Presented by Dr. Douglas Macfarlan:

Early faradic machine for electro-therapy of muscular paresis and paralysis.

Presented by Mr. Anthony P. Mynders, member of the Board of Directors of American Foundation for Better Hearing, through the interest of Dr. Douglas Macfarlan, a collection of audiometers and hearing aids, as follows:

Sonotone-Jones-Knudsen Audiometer and accessions (1924)

Maico Audiometer and accessions (1937)

Electric stethoscope

Two early Maico hearing aids with batteries (1940)

The latest miniature Maico hearing aid with end piece microphone

Printed circuit and two miniature tubes

Maico Monopack hearing aid of about 1948, with batteries

Maico all in one hearing aid

Ear moulds

Earrings to hold hearing aid receivers

First Maico all in one hearing aid (1945)
Three sizes of tubes used in hearing aids
Set of batteries used in hearing aids
Stethotron, an electric stethoscope

Presented by Dr. Mortimer Herzberg:

Autopsy set formerly belonging to Dr. Thomas Hollingsworth Andrews, Demonstrator of Anatomy at Jefferson Medical College.

Photographs of the presentation of the collection of hearing aids by Mr. Anthony P. Mynders to Dr. Douglas Macfarlan, acting for the chairman, were taken, and later appeared in *The Hearing Dealer*. A motion picture film was also made and later appeared in a newsreel on station WFIL-TV.

R. Philip Custer
Chairman

The College Collections

Mrs. Ella N. Wade was reappointed custodian of College Collections.

The portraits of Wharton Sinkler, M.D., and Frederick P. Henry, M.D., were cleaned, restored and varnished.

Accessions to College Collections were as follows:

Presented by Dr. Burton Chance:

A large collection of ancient, old and modern spectacles

Presented by Dr. Samuel X Radbill:

Certificate of the College of Physicians of Philadelphia presented to its first vice-president, John Jones, dated 1787.

Presented by Dr. William G. Leaman, Jr.:

Large bronze plaque by R. Tait McKenzie of the Relay Carnival of the University of Pennsylvania, founded in 1895.
Bronze medal of David Hosack
Bronze medal of J. L. R. Agassiz

Presented by Dr. Alfred C. Wood:

Gold and onyx cuff links formerly belonging to Dr. Alfred Stillé

Presented by Dr. William E. Robertson:

Bleeding lancet formerly belonging to Dr. Charles Toothaker

Presented by Dr. J. Monroe Thorington:

Small male athletic figure made by R. Tait McKenzie

Presented by Dr. Theodore F. Bach:

Loring ophthalmoscope formerly belonging to Dr. Minnie Stryker (1869–1950), Medical Missionary to China.
Bowles' stethoscope, also formerly belonging to Dr. Stryker.

Presented by Mr. Joseph R. Stulb:

Two gold-headed and gold-trimmed canes formerly belonging to Professor Edward T. Reichert, Professor of Physiology at the University of Pennsylvania.

R. Philip Custer
Chairman

Report of the Publication Committee

THE chief change to be recorded in connection with the four issues under review (vol. 18, nos 3 and 4; vol. 19, nos 1 and 2) was a change in the cover date of the issues. To meet the Post Office's demand, the cover dates were altered to accord with what had been for years the actual dates of mailing. Thus, what had been called the June issue (though customarily mailed out in August) became the August issue, and subsequent issues will follow suit. The four issues of the annual volume will, therefore, hereafter be dated (no. 1) June, (no. 2) August, (no. 3) February, (no. 4) April (the months of their actual mailing), instead of as formerly, April, June, December, February. The change is one which should cause general satisfaction among those having anything to do with the journal.

The four issues contained ten more pages than last year's series. The reason is that all but one of the College's endowed lectures were made available, and a number of them were as substantial in length as in quality. We would be remiss if we did not gratefully acknowledge the assistance given us, in this respect, by the Executive Secretary, Dr. J. Harold Austin, who so successfully undertook the ungrateful task of rounding up the sometimes elusive manuscripts. Again, our labors were far less laborious than they might have been, thanks to the clerk of the Section on General Medicine (Dr. John Lansbury), who regularly delivered the Section's abstracts to us while the bodies were still comfortably warm.

It is a matter of regret that historical studies occupied so few of our pages in this series, since the College is one of the few institutions with membership and library resources equipped to keep us reminded that medicine is not a science isolated from the general history of mankind. We confidently anticipate, however, that more "Studies" of this sort will be appearing in the following series, to uphold the post-ampersand substantive in the journal's title.

Approved:

DAVID A. COOPER
Chairman

W. B. MCDANIEL, 2d
Editor

Annual Reports of the Sections*

General Medicine

The Section had a membership of 150. The average number of members attending each of the seven meetings was 75.

Abstracts of all the presentations, except those at the joint meeting in January, will be found in the *Transactions & Studies*.

John Lansbury
Clerk

Medical History

During the year 1951, 108 Fellows became active members of the Section, an increase of 18 over the previous year.

The 1950 officers were re-elected, and Dr. T. Grier Miller who also has taken an active part in the affairs of the Section, reappointed the same executive committee. Under this regime, three stated meetings of the Section were held at the Hall of the College, the programs of which appeared in the August number of our *Transactions & Studies*. The entire proceedings of the third meeting, that devoted to the late Dr. Francis R. Packard and the two hundredth anniversary of the founding of The Pennsylvania Hospital, were published in the same number. The papers read by Dr. William W. Cadbury and Dr. Nicholas Padis at the second meeting will also be published in the journal of the College. The first two meetings were each attended by 40 or more, while the Packard meeting drew an audience of over 100.

Continuing the policy of previous years, the Section, with the financial support of the five Philadelphia medical colleges, arranged another course of six weekly one-hour lectures on medical history for the students of medicine of this city. This course was identical with the one given last year. The total attendance for the six lectures was 1,367, approximately the same as last year. Mimeographed outlines of each lecture were again prepared, through the good offices of our executive secretary, Dr. J. Harold Austin, and the clerk of the College, Miss Olga E. Lang. These were distributed to the students in attendance, together with mimeographed notes explaining the exhibits prepared for each lecture from our own historical resources by our enthusiastic and hard working librarian, Dr. Walton B. McDaniel, 2nd. An innovation this year was a pertinent exhibit of old medical instruments and armamentaria from the Mütter Museum prepared by the curator, Mrs. Ella N. Wade. This arrested the attention and elicited much curious comment from everybody going past the exhibit as they entered Mitchell Hall for the lectures. The wholehearted cooperation of the deans of the different medical schools is an important stimulus needed to maintain student attendance. The course is now announced by most of the schools in their annual bulletins. Obviously, these special lectures in medical history should be continued.

While not strictly an activity of our Section on Medical History it might be of interest to mention at this point a course of four historical lectures delivered for the Department of Dermatology of the Graduate School of Medicine of the University of Pennsylvania. This course was arranged by Dr. Herman Beerman, Chairman of the department, and a member of our Section on Medical History. Other members of our Section who participated in this course were Drs. Joseph V. Klauder and Samuel X Radbill. Attendance by the graduate students was required. They were especially gratified with the lectures in view of the fact that candidates for certification by The American Board of Dermatology had received some questions dealing with the history of their specialty. Much interest was evidenced in a display of books and records dealing with the history of dermatology.

* For the programs of the Sections in 1951, see the *Transactions & Studies*, vol. 19, no. 2, August, 1951, and elsewhere in this issue (vol. 19, no. 4, April, 1952).

Inspired by the success of this course, Dr. John P. Scott, Chairman of the Department of Pediatrics of the Graduate School of Medicine of The University of Pennsylvania inaugurated a similar venture when three historical lectures were given by the Clerk of the Section this year to the graduate students in pediatrics.

On May 3rd to 5th, Dr. William G. Leaman, Jr., attended the meeting of the American Association of Medical History at Baltimore, Maryland, at his own expense, as delegate from the Section on Medical History of the College of Physicians of Philadelphia. Among other Fellows from our Section who attended this meeting were Drs. Esmond R. Long, Robert J. Hunter and Samuel X Radbill. The Section was active in founding the national association and continues to take a sincere interest in its success.

SAMUEL X RADBILL
Clerk

OPHTHALMOLOGY

Membership in the Section was 63, of whom 61 paid their dues. The average attendance at the first six of the seven meetings was 98.

The Fourteenth Annual de Schweinitz Lecture was delivered by Dr. Peter C. Kronfeld, of Chicago, November 15th.

The Zentmayer Prize was awarded to Dr. I. H. Leopold, Dr. Arthur H. Keeney, and Virginia T. Keeney, B. S., for their paper, "Studies of Capillary Phenomena in Primary Glaucoma"; and to Drs. Samuel De Long and Harold G. Scheie, for their paper, "Dibenamine: a Clinical and Experimental Study".

M. LUTHER KAUFFMAN
Clerk

OTOLARYNGOLOGY

The Section consists of 59 members and 3 honorary members. Average attendance at the first five of the six meetings (including the joint meeting, in March, with the Section of Otolaryngology of the New York Academy of Medicine, held in New York) was 51.

Dr. Robert J. Hunter presented to the Section, for deposit in the College library, a volume of notes on the course in otolaryngology given by Dr. E. B. Gleason at the Medico-Chirurgical College, in 1901, taken by Dr. L. Loutfian, of Turkey.

The Section purchased, for the College Library, Codronchius' *De vitiis vocis, libri duo*, Frankfurt, 1597, the first published monograph on diseases affecting the voice.

M. VALENTINE MILLER
Clerk

PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

The Section, which has a membership of twenty-seven, held three meetings in 1951. Dr. Norman R. Ingraham, Jr.'s paper, "Newer Developments in Venereal Disease Control in the United States and Abroad", read at the first meeting, has already been published in the College's *Transactions & Studies*. The paper was discussed by Drs. Klauder, Appleton, and Lucchesi. The second paper, "The Philadelphia Public Health Survey—Present and Future Aims", by Mr. Clyde Arbegast, Consultant, Health Division, Health and Welfare Council, reviewed the aims and accomplishments of the survey. The meeting was attended by about 40 persons.

At the second meeting, Dr. Dorland J. Davis, Executive Secretary of the Influenza Information Center, Bethesda, Md., spoke on "New Approaches to the Epidemiology of Influenza". He reviewed the nature of the influenza epidemics which occurred in the past years and noted that there was a definite decrease in the mortality rate. He reviewed the functions of the Influenza Information Center and the procedures by which information about epidemics is obtained. The second speaker, Dr. Angelo M. Perri, chief of the Division of Communicable Disease Control, reviewed the epidemics of influenza as they occurred in Philadelphia and the significance of reports made to the Health Department. Dr. L. P. Kravis, University of Pennsylvania School of Medicine, discussed various laboratory procedures for diagnosis, and the results obtained from vaccines in a pilot study by using only 0.1 cc. of

vaccine instead of the recommended full dose. The fourth speaker, M. Michael Sigel, Ph.D., University of Pennsylvania School of Medicine, questioned the existence of Type C virus and discussed methods by which the diagnosis could be made rapidly, so that the indications for immunization could be established. The papers were discussed by Dr. Stuart Mudd and Dr. Schrack. Twenty-six persons attended the meeting.

The third meeting was held jointly with Region No. 1 of the Pennsylvania Public Health Association. The guest speaker, Dr. E. M. Holmes, Jr., Director of Public Health, Richmond, Virginia, spoke on "Multiphasic Health Examinations". His paper has been accepted for publication in the College's *Transactions & Studies*. The paper was discussed by Drs. Solis-Cohen, Boucot, and Aston. Dr. Harold L. Israel, University of Pennsylvania Graduate School of Medicine, the second speaker, reviewed the nature of pulmonary disease and the changing picture in the etiology of various types of pulmonary disorders. He also commented on the influence of the antibiotics on pulmonary diseases and mortality, and intimated that bronchiectasis may have various etiologies which are not apparent at present, and that little is known about the course and prognosis of this condition. He stated that fungus infections of the lung are rare in this region. Drs. Arnett and Sigel commented on this paper. Twenty-three persons attended the meeting.

At the business meeting following this program, there was discussion of ways and means by which interest could be stimulated in public health matters and in attendance at the meetings of the Section. The matter was referred to the newly elected officers, Dr. A. C. LaBoccetta, chairman, and Dr. Katherine Boucot, clerk.

A. C. LaBoccetta
Clerk

List of College Lectures, 1951

3 January 1951

HARVEY, A. MCGEHEE. Adrenal Cortical Activity and the Hypersensitive State: Some Clinical and Experimental Observations (Mary Scott Newbold Lecture LXIV, printed in the *Transactions & Studies*, August, 1951.)

7 February 1951

SIMMONS, JAMES STEVENS. Public Health As a Weapon for National Defense (James M. Anders Lecture XXV, printed in the *Transactions & Studies*, April, 1951.)

7 March 1951

The Present Status of ACTH and Cortisone, FRANCIS D. W. LUKENS, *moderator*. PASCHKIS, KARL E. Physiological Effects and Clinical Indications; LANSBURY, JOHN. Administration and Contra-indications; HOLLANDER, JOSEPH LEE. Problems of Long Term Administration. (Joint meeting with the Philadelphia County Medical Society, program arranged by the Society.)

4 April 1951

POOL, J. LAWRENCE. Topectomy, 1946–1951: Report on 106 Consecutive Non-project Topectomy Operations (Nathan Lewis Hatfield Lecture XXXV, printed in the *Transactions & Studies*, August, 1951).

2 May 1951

PERKINS, WILLIAM H. The Value of Health Centers to the Community (James M. Anders Lecture XXVI, printed in the *Transactions & Studies*, February, 1952).

3 October 1951

THORN, GEORGE W. The Adrenals in Health and Disease (Alvarenga Prize Lecture XI, printed in the *Transactions & Studies*, February, 1952).

7 November 1951

WOLFERTH, CHARLES C. Adrenalectomy in Relation to Hypertension (Mary Scott Newbold Lecture LXV, printed in the *Transactions & Studies*, April, 1952). (Joint meeting with the Philadelphia County Medical Society.)

5 December 1951

CLERF, LOUIS H. Historical Aspects of Foreign Bodies in the Air and Food Passages (Thomas Dent Mütter Lecture LXIV, to be printed in the *Transactions & Studies*).

Officers, Committees, Sections, and Administrative Staff of the College 1952

President

Richard A. Kern

Vice-President

Lewis C. Scheffey

Secretary
Leandro M. Tocantins

Treasurer
Francis C. Grant

Censors

John H. Gibbon
Edward B. Krumbhaar
O. H. Perry Pepper
J. Parsons Schaeffer

Honorary Librarian
William Egbert Robertson

Ex-Presidential Councillor
T. Grier Miller

Elected Councillors

To serve until January, 1953
Thomas M. Durant
Gilson C. Engel

To serve until January, 1954
Louis H. Clerf
William G. Leaman, Jr.

To serve until January, 1955
William L. Martin
Francis C. Wood

Council

The forenamed and the chairmen of the Standing Committees*

ELECTIVE STANDING COMMITTEES

Library

Truman G. Schnabel, *ch'n*
John F. Huber
Jonathan E. Rhoads
Charles Rupp
Carroll S. Wright

Hall

L. Kraeer Ferguson, *ch'n*
Edward S. Dillon
Catharine Macfarlane
John B. Montgomery
Joseph B. VanderVeer

Mütter Museum and College Collections

R. Philip Custer, *ch'n*
Theodore F. Bach
Peter A. Herbut

Publication

David A. Cooper, *ch'n*
Ernest E. Aegerter
Lawrence S. Carey

* The President is a member *ex officio* of all Standing Committees.

APPOINTIVE STANDING COMMITTEES

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Charles L. Brown
Glen G. Gibson
The Treasurer, *ex officio*

Entertainments

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Harold G. Scheie
Barton R. Young

Scientific Business

Jonathan E. Rhoads, *ch'n*
Kenneth E. Appel
Henry L. Bockus
R. Philip Custer
Garfield G. Duncan
Theodore R. Fetter
Malcolm W. Miller
Jesse T. Nicholson
Donald M. Pillsbury
The Secretary, *ex officio*

Public Health, Preventive Medicine and Public Relations

Theodore R. Fetter, *ch'n*
Samuel B. Hadden
Walter P. Havens, Jr.
Norman R. Ingraham, Jr.
David S. Polk

PRIZE COMMITTEES AND TRUSTEES

Alvarenga Prize and Lectureship

Henry L. Bockus, *ch'n*
O. Spurgeon English
Robert A. Kimbrough, Jr.
Karl E. Paschkis
William C. Stadie

Weir Mitchell Oration

Kenneth E. Appel, *ch'n*
John V. Blady
John H. Gibbon, Jr.
Eugene P. Pendergrass
Joseph Stokes, Jr.

Trustee under the Will of Thomas Skelton Harrison

J. Parsons Schaeffer

Honorary Director of the Department of Medical Arts

Samuel B. Sturgis

Nathan Lewis Hatfield Prize and Lectureship

Jesse T. Nicholson, *ch'n*
Henry P. Royster
H. Curtis Wood, Jr.

Mary Scott Newbold Lectures

Malcolm W. Miller, *ch'n*
John H. Gibbon, Jr.
J. Robert Willson
The President and the Chairman of the Committee on Scientific Business, *ex officiis*

Trustees of Nathan Lewis Hatfield Prize and Lectureship

William D. Stroud
J. Montgomery Deaver
Thomas Fitz-Hugh, Jr.

Honorary Legal Counsel

Eric A. McCouch

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William A. Jeffers, *ch'n*
John Lansbury, *clerk*
Executive Committee: Charles L. Brown, William G. Leaman, Jr., Leandro M. Tocantins

Medical History

Herbert T. Kelly, *ch'n*
Samuel X Radbill, *clerk*
Executive Committee: Maurice S. Jacobs, Louis B. Laplace, William G. Leaman, Jr.

Ophthalmology

George F. J. Kelly, *ch'n*
M. Luther Kauffman, *clerk*
Executive Committee: Burton Chance, Perce DeLong, Wilfred E. Fry

Otolaryngology

M. Valentine Miller, *ch'n*
Benjamin Shuster, *clerk*
Executive Committee: Oscar V. Batson, Louis H. Clerf, Robert J. Hunter

Public Health, Preventive and Industrial Medicine

Alfred C. LaBoccetta, *ch'n*
Katharine R. Boucot, *clerk*
Executive Committee: David A. Cooper, Charles-Francis Long*, Pascal F. Lucchesi

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ADMINISTRATIVE STAFF OF THE COLLEGE

Executive Secretary

J. Harold Austin

Librarian and Editor

W. B. McDaniel, 2d

Administrative Assistant Librarian

Elliott H. Morse

Curator of the Mütter Museum and Custodian of the College Collections

Mrs. Ella N. Wade

Clerk of the College

Olga E. Lang

Superintendent

Alfred F. Nelson**

* Died, 28 Feb. 1952.
** Died, 23 Feb. 1952.

Fellows

December 31, 1951

ELECTED

1948. Adelizzi, Richard A., 1723 S. Broad St.
1926. Adler, Francis Heed, 313 S. 17th St.
1949. Aegerter, Ernest E., 3400 N. Broad St.
1914. Aiken, Thomas G., Berwyn, Pa.
1936. Alexander, Fay Knight, Germantown Professional Bldg., Greene and Coulter Sts.
1947. Allbritten, Frank F., Jr., 1025 Walnut St.
1906. Allen, Francis Olcott, Jr., Secane, Pa.
1932. Allen, Frederick H., 1711 Fitzwater St.
1935. Alpers, Bernard J., 111 North 49th St.
1930. Appel, Kenneth E., 111 N. 49th St.
1905. Appleman, Leighton Francis, 308 S. 16th St.
1935. Armitage, George L., 400 E. 13th St., Chester, Pa.
1922. Arnett, John H., 2116 Pine St.
1942. Aronson, Joseph D., Henry Phipps Institute, 7th and Lombard Sts.
1920. Astley, G. Mason, 812 N. 63rd St.
1944. Atkins, Joseph P., 1201 Knox Rd., Wynnewood, Pa.
1935. Atlee, John L., Jr., 37 E. Orange St., Lancaster, Pa.
1914. Austin, J. Harold, 19 S. 22nd St.
1935. Bach, Theodore F., 1900 Rittenhouse Sq.
1942. Bachman, Carl, Univ. of Pa. Hospital.
1937. Bacon, Emily P., 1930 Chestnut St.
1946. Baker, Walter W., 255 S. 17th St.
1940. Barba, Philip S., 222 W. Harvey St.
1943. Barden, Robert P., 8835 Germantown Ave.
1911. Barnard, Everett P., 1820 Rittenhouse Sq.
1939. Barnshaw, Harold D., 406 Cooper St., Camden, N. J.
1939. Bartle, Harvey, Jr., 133 S. 36th St.
1931. Bates, William, 2029 Pine St.
1932. Batson, Oscar V., 3502 Hamilton St.
1921. Bauer, Edward L., 1609 Spruce St.
1933. Bauer, John T., 312 E. Second St., Moorestown, N. J.
1939. Baumann, Frieda, 1930 Chestnut St.
1908. Beardsley, E. J. G., 1919 Spruce St.
1930. Beardwood, Joseph T., Jr., 2031 Locust St.
1949. Beecham, Clayton T., Greene & Coulter Sts.
1935. Beerman, Herman, 2422 Pine St.
1942. Behrend, Albert, 255 S. 17th St.
1945. Behrend, Bernard, 5910 Greene St.
1934. Behrend, Moses, 255 S. 17th St.
1949. Beizer, Lawrence H., 255 S. 17th St.
1930. Belk, William Parks, Times Medical Bldg., Ardmore, Pa.
1936. Bell, Benjamin Tertius, Abington Memorial Hospital, Abington, Pa.
1947. Bellet, Samuel, 2021 Spruce St.
1943. Berk, J. Edward, 255 S. 17th St.
1951. Bernstine, Jacob B., 255 S. 17th St.
1941. Bernstein, Mitchell, 1321 Spruce St.

1937. Bertolet, J. Allen, 1530 Locust St.
1934. Biddle, Sydney Geoffrey, 255 S. 17th St.
1918. Billings, Arthur E., 2020 Spruce St.
1949. Bishop, Edward H., 255 S. 17th St.
1933. Bishop, Paul A., Pennsylvania Hospital.
1944. Blady, John V., 340 Fishers Rd., Bryn Mawr, Pa.
1951. Blank, Harvey, c/o E. R. Squibb & Sons, 745 Fifth Ave., New York 22, N. Y.
1917. Block, Frank B., 305 Tabor Medical Bldg., York & Tabor Rds.
1949. Blumstein, George I., 2039 Delancey St.
1929. Bockus, Henry L., 250 S. 18th St.
1928. Boles, Russell S., Rittenhouse Plaza, 1901 Walnut St.
1923. Bond, Earl D., 111 N. 49th St.
1911. Bonney, Charles W., 255 S. 17th St.
1948. Bookhammer, Robert S., 2031 Locust St.
1931. Bortz, Edward Le Roy, 2021 W. Girard Ave.
1921. Borzell, Francis Frank, 4940 Penn St.
1936. Bostwick, Delazon Swift, 106 Linwood Ave., Ardmore, Pa.
1928. Bothe, Albert E., 225 S. 17th St.
1928. Bothe, Frederick A., 255 S. 17th St.
1951. Boucot, Katharine R., 229 W. Upsal St.
1947. Bourland, Henry, 2219 Garret Rd., Drexel Hill, Pa.
1923. Bower, John O., 2008 Walnut St.
1942. Bowie, Morris A., Rosemont, Pa.
1907. Bradley, William Nathaniel, 1725 Pine St.
1942. Branen, William, Whitby & Cypress Ave., Yeadon, Pa.
1921. Bransfield, John W., 2101 Spruce St.
1948. Braun, William, 406 Cooper St., Camden, N. J.
1951. Brinton, S. Jervis, Fishers Road, Bryn Mawr, Pa.
1946. Briscoe, Clarence Conway, 255 S. 17th St.
1917. Bromer, Ralph S., 318 Milbank Road, Bryn Mawr, Pa.
1936. Brown, Charles L., 1030 Indian Creek Rd.
1936. Brown, Clark, E., Lankenau Hospital.
1932. Brown, Claude P., 1930 Chestnut St.
1919. Brown, Henry P., Jr., Willow Grove & Cherokee Avenues.
1939. Brust, Raymond W., 4710 Chester Ave.
1943. Buerki, Robin C., University of Pa.
1940. Burnett, W. Emory, 3401 N. Broad St.
1941. Butler, Miriam, 1930 Chestnut St.
1906. Butler, Ralph, 47th & Pine Sts.
1907. Cadwalader, Williams B., 133 S. 36th St.
1928. Campbell, Edward H., 133 S. 36th St.
1944. Campion, Richard J., Penllyn Rd., Springhouse, Ambler, Pa.
1931. Cantarow, Abraham, 1025 Walnut St.
1935. Carey, Lawrence S., 330 S. 9th St.
1931. Cariss, Walter L., 2043 Walnut St.
1930. Carpenter, Chapin, 1930 Chestnut St.
1905. Carpenter, Herbert B., 1805 Spruce St.
1926. Carpenter, Howard Childs, 1805 Spruce St.
1917. Carson, John B., 1802 Pine St.
1922. Case, Eugene A., 63 W. La Crosse Ave., Landsdowne, Pa.
1937. Castallo, Mario A., 1621 Spruce St.
1943. Castigliano, S. Gordon, 853 Mt. Pleasant Rd., Bryn Mawr, Pa.
1949. Caswell, H. Taylor, Greene & Coulter Sts.

1950. Chamberlain, Richard H., 3400 Spruce St.
1933. Chamberlain, W. Edward, Temple University Hospital.
1939. Chamberlin, George W., Reading Hospital, Reading, Pa.
1900. Chance, Burton, 317 S. 15th St.
1945. Chance, Burton, Jr., 1726 Spruce St.
1948. Chapman, John P., Lincoln-Liberty Building, Broad & Chestnut Sts.
1950. Chapple, Charles C., 570 E. Evergreen Ave., Chestnut Hill, Pa.
1939. Charr, Robert Kyun Hyun, 2038 Locust St.
1947. Chouké, Kehar S., P.O. Box 547, Kecoughton, Va.
1945. Cianfrani, Theodore, 1930 Chestnut St.
1939. Ciccone, Emmet F., 2021 Murray St.
1951. Clagett, Augustus H., Jr., U. S. Veterans Administration Hosp., Wilmington, Del.
1929. Clark, Eliot R., 315 S. 41st St.
1934. Clark, Jefferson Hamer, 101 Maple Ave., Wyncote, Pa.
1951. Clark, John K., University Hospital, 36th & Spruce Sts.
1947. Clark, Thomas Williams, 400 E. Willow Grove Ave.
1947. Classen, Charles H., Cushman Rd. and Lancaster Ave., Rosemont, Pa.
1926. Clerf, Louis H., 1530 Locust St.
1910. Cloud, J. Howard, 111 St. Pauls Road, Ardmore, Pa.
1903. Coates, George Morrison, 1721 Pine St.
1908. Codman, Charles A. E., S.E. Corner 42d and Spruce Sts.
1941. Cohen, J. Gershon, 255 S. 17th St.
1949. Cohen, Louis, 255 S. 17th St.
1949. Cohen, Louis B., 1320 Arrott St.
1951. Cohen, Leon Solis-, 1422 Chestnut St.
1907. Cohen, Myer Solis-, 2110 Spruce St.
1934. Colgan, Robert C., 5882 N. Marshall St.
1934. Collins, Leon Howard, Jr., 133 S. 36th St.
1943. Colonna, Paul C., Univ. of Pa. Hospital.
1949. Conger, Kyril B., 3401 N. Broad St.
1945. Coonel, Pauline, 47 E. Mt. Pleasant Ave.
1930. Cooper, David A., 1520 Spruce St.
1947. Coppolino, John F., 1807 S. Broad St.
1941. Cornelius, Chalmers E., 119 Summit Ave., Jenkintown, Pa.
1911. Cornell, Walter S., Board of Public Education, Parkway and 21st St.
1945. Corrigan, Patrick H., 1720 S. Broad St., Trenton, N. J.
1914. Corson, Edward F., 136 S. 16th St.
1946. Costello, Thomas J., 131 Pennsylvania Avenue, Bryn Mawr, Pa.
1924. Cowan, Alfred, 1930 Chestnut St.
1940. Cowan, Thomas H., 1930 Chestnut St.
1904. Craig, Frank A., The Henry Phipps Institute, 7th and Lombard Sts.
1907. Crampton, George S., 2031 Locust St.
1947. Crane, A. Reynolds, 807 Spruce St.
1937. Crane, Martin P., 2412 N. Broad St.
1920. Creighton, William J., 37 S. 20th St.
1941. Creskoff, Adolph J., 3400 Spruce St.
1920. Cross, George H., Chester, Pa.
1917. Cross, Sumner H., P. O. Box 126, Jenkintown, Pa.
1921. Crossan, Edward T., 5324 Wayne Ave.
1904. Cruice, John M., 407 S. 22nd St.
1937. Crump, Jean, 1930 Chestnut St.
1937. Curtis, Lawrence, 255 S. 17th St.
1934. Custer, R. Philip, 221 Walnut Ave., Wayne, Pa.

1938. Dannenberg, Arthur M., 235 S. 15th St.
1951. Daugherty, Earl A., 2025 W. Girard Ave.
1947. Davis, C. Nelson, 133 South 36th St.
1936. Davis, David M., 255 S. 17th St.
1937. Davis, Perk Lee, 255 S. 17th St.
1951. Davis, J. Wallace, 135 S. 18th St.
1935. Deaver, J. Montgomery, 1830 Delancey Pl.
1947. Dehne, Theodore L., Adams Avenue and Roosevelt Blvd.
1902. Dehoney, Howard, 240 S. 13th St.
1935. Deibert, Irvin Elmer, 538 Cooper St., Camden, N. J.
1948. Deichler, John W., 1930 Chestnut St.
1923. De Long, Perce, 37 S. 20th St.
1951. De Palma, Anthony F., 255 S. 17th St.
1928. Dewees, A. Lovett, Glen Mills, Del. Co., Pa.
1924. Dillon, Edward S., 2028 Delancey Pl.
1932. Dintenfass, Henry, 1305 Spruce St.
1920. Doane, Joseph C., 617 W. Hortter St.
1948. Dohan, Francis Curtis, 80 Princeton Road, Cynwyd, Pa.
1946. Donnelly, Andrew J., 33rd and Powelton Ave.
1942. Donnelly, Edward J., 1321 Spruce St.
1933. Donnelly, Joseph C., 255 S. 17th St.
1937. Donnelly, Robert T. M., 255 S. 17th St.
1910. Drayton, William, Jr., 1930 Spruce St.
1949. Dripps, Robert D., 3400 Spruce St.
1935. Duane, William, Jr., 2100 Walnut St.
1944. Dublin, George J., 1930 Chestnut St.
1944. Dugger, John H., 3902 Vaux St.
1935. Duncan, Garfield G., 330 S. 9th St.
1937. Dunn, Charles W., 265 S. 19th St.
1951. Dunne, Francis S., 133 S. 36th St.
1942. Durant, Thomas M., 3401 N. Broad St.
1947. Durkin, John Keenan, 34 W. Montgomery Ave., Ardmore, Pa.
1942. Dyer, W. Wallace, Univ. of Pa. Hospital.
1935. Eads, John T., 2029 Delancey St.
1911. Earnshaw, Henry C., Bryn Mawr, Pa.
1936. Easby, Mary Hoskins, Woman's Hospital.
1948. Eaton, Francis H., 4007 Chestnut St.
1937. Edeiken, Joseph, 2130 Delancey Pl.
1944. Eger, Sherman A., 2029 Delancey St.
1949. Egoville, John W., 720 W. 63rd St.
1944. Ehrich, William E., 540 W. Hortter St.
1930. Eiman, John, Cynwyd, Pa.
1946. Elfman, Louis Kenneth, 6330 Lebanon Avenue.
1949. Elkinton, J. Russell, Oak Lane, Moylan, Pa.
1951. Ellis, Mackinnon., Bryn Mawr Ave., Bryn Mawr, Pa.
1939. Ellis, Van Mashburn, 1530 Locust St.
1928. Ellison, Richard T., 269 S. 19th St.
1936. Ellson, J. Vernon, Glendale Rd. & Chestnut St., Upper Darby, Pa.
1904. Elmer, Walter G., 1801 Pine St.
1937. Elsom, Kendall A., 133 S. 36th St.
1934. Ely, William C., 3912 Chestnut St.
1932. Engel, Gilson C., 255 S. 17th St.
1945. English, O. Spurgeon, 3401 N. Broad St.

1942. Erb, William H., 133 S. 36th St.
1950. Ersner, Matthew S., 1915 Spruce St.
1948. Everts, Glenn S., 5515 Wissahickon Ave., Apt. D-403.
1946. Farell, David M., 1912 Spruce St.
1903. Farr, Clifford B., Bryn Mawr, Pa.
1945. Farrar, George Elbert, Jr., 528 Scott Rd., Gladwyne, Pa.
1930. Farrell, John T., Jr., 255 S. 17th St.
1935. Ferguson, Lewis Kraeer, 133 S. 36th St.
1936. Fetter, Ferdinand, 322 S. 21st St.
1945. Fetter, John S., High Rd. at Welsh Rd., Huntingdon Valley, Pa.
1935. Fetter, Theodore R., 255 S. 17th St.
1924. Fewell, Alexander G., 1924 Pine St.
1943. Finkelstein, Arthur, 480 Latch's Lane, Merion, Pa.
1947. First, Arthur, 1714 Spruce St.
1945. Fiske, Frederick A., 1530 Locust St.
1928. Fitz-Hugh, Thomas, Jr., 2016 Delancey Pl.
1928. Flick, John B., 330 S. 9th St.
1939. Flippin, Harrison F., 255 S. 17th St.
1951. Ford, Elbert, S. C., 255 S. 17th St.
1941. Fox, C. Calvin, 1806 Spruce St.
1906. Fraley, Frederick, 71st and City Line, Overbrook, Pa.
1941. Frazier, William Doane, 133 S. 36th St.
1951. Friedland, Carl K., 133 S. 36th St.
1951. Friedman, Paul Sigmund, 1422 Chestnut St.
1942. Friedman, Reuben, 877 N. 6th St.
1933. Fritch, James Scott, 269 S. 19th St.
1937. Fritz, Herbert H., Pennswood Rd., Bryn Mawr, Pa.
1940. Fry, Kenneth E., 255 S. 17th St.
1935. Fry, Wilfred Eyles, 1930 Chestnut St.
1937. Furlong, Thomas F., Jr., Times Medical Building, Ardmore, Pa.
1935. Gammon, Geo. D., Univ. of Pa. Hospital.
1951. Garlichs, Richard W., 216 N. Manoa Road, Havertown, Pa.
1931. Garner, Vaughn C., Germantown Professional Building.
1950. Garvin, Eugene J., 4219 Baltimore Ave.
1935. Geist, Donald C., 1930 Chestnut St.
1899. Gibbon, John H., Media, Pa.
1934. Gibbon, John H., Jr., 1025 Walnut St.
1939. Gibson, Glen Gregory, 2031 Locust St.
1944. Gifford, Edward S., Jr., 1913 Spruce St.
1920. Gill, A. Bruce, 1930 Chestnut St.
1927. Gilmour, William R., 413–14 Weightman Bldg., 1524 Chestnut St.
1949. Ginsburg, Isadore W., 3401 N. Broad St.
1931. Giordano, Anthony A. S., 1819 S. Broad St.
1945. Goldberg, Samuel J., 1723 Pine St.
1933. Goldburgh, Harold L., 1932 Spruce St.
1935. Goldsmith, N. Ralph, 1351 Tabor Rd.
1949. Gopadze, Illarion I., 1809 Delancey Pl.
1905. Gordon, Alfred, 1520 Spruce St.
1928. Gordon, Burgess L., 1832 Spruce St.
1937. Gordon, William, 5345 Spruce St.
1941. Gouterman, Joseph I., 1930 Chestnut St.
1894. Graham, Edwin E., 1713 Spruce St.
1926. Grant, Francis Clark, Univ. of Pa. Hospital.

1940. Greene, Lloyd B., 136 S. 16th St.
1950. Gregory, John E., 235 N. 15th St.
1934. Griffith, John Q., Jr., 6 N. Fredericksburg Ave., Margate, N. J.
1945. Griffiths, John E., Mermont Apartments, Bryn Mawr, Pa.
1941. Groff, Robert A., 1930 Chestnut St.
1933. Gruber, Charles M., 128 Overhill Rd., Cynwyd, Pa.
1932. Guequierre, Jacques P., Mermont Plaza, Bryn Mawr, Pa.
1945. György, Paul, Univ. of Pa.
1935. Hadden, Samuel B., 37 S. 20th St.
1951. Hafkenschiel, Joseph H., 3600 Spruce St.
1945. Hahn, George A., 255 S. 17th St.
1935. Haines, Harlan F., 134 S. State Rd., Upper Darby, Pa.
1951. Hallett, Joseph W., 1001 Medical Arts Bldg., 16th & Walnut Sts.
1939. Hamblock, Leonard C., 1632 Spruce St.
1938. Hand, John G., 1724 Pine St.
1947. Hanes, William James, 218 E. Beechtree Lane, Wayne, Pa.
1951. Harkins, Herbert P., 1930 Chestnut St.
1932. Harris, Stanley E., 229 Maple Ave., Delanco, N. J.
1948. Harris, T. N., 2222 N. 53rd St.
1929. Harrison, Francis G., 1900 Spruce St.
1933. Harrison, William John, 135 S. 17th St.
1926. Hartmann, Fred L., 1914 Pine St.
1946. Harvey, Edith E., 406 York Rd., Jenkintown, Pa.
1947. Harvey, Rolfe Marsh, Glenmary & Houston Rds., Radnor, Pa.
1935. Haskell, Benjamin F., 1426 Spruce St.
1946. Hatfield, C. Alexander, 330 S. 9th St.
1947. Havens, Walter Paul, Jr., 300 Cherry Lane, Wynnewood, Pa.
1947. Hawthorne, Herbert Reid, 250 S. 18th St.
1911. Heed, Charles R., College Ave. & Coopertown Rd., Haverford, Pa.
1946. Hendrickson, Frank O., 37 S. 20th St.
1944. Herbut, Peter A., Jefferson Medical College Hospital.
1927. Herman, Leon, 136 S. 16th St.
1951. Herrman, Clinton S., 255 S. 17th St.
1944. Hershey, J. Ivan, 935 Bowman Ave., Wynnewood, Pa.
1924. Hewson, William, 1614 Locust St.
1949. Heyl, W. Meredith, 100 W. Coulter St.
1924. Hirst, John C., 2d, 500 N. 20th St.
1943. Hitschler, William J., 8840 Germantown Ave.
1944. Hneleski, Ignatius S., 802 S. 48th St.
1943. Hockaday, Agnes, 316 Shadeland Ave., Drexel Hill, Pa.
1939. Hodes, Philip J., Univ. of Pa. Hospital.
1947. Hodges, John H., 1025 Walnut St.
1948. Hoffman, George L., Jr., 133 S. 36th St.
1949. Hollander, Joseph L., 36th & Spruce Sts.
1932. Hollingsworth, I. Pemberton, 411 N. Walnut St., West Chester, Pa.
1951. Hollis, Charles B., 1930 Chestnut St.
1949. Hopkins, Henry U., 4526 Osage Ave.
1946. Horan, Gerald W., 5819 Chester Ave.
1950. Horn, Robert C., 57 Berkley Ave., Lansdowne, Pa.
1947. Horwitz, Orville, 133 S. 36th St.
1950. Houlihan, Carl T., 728 S. 60th St.
1944. Housel, Edmund L., 255 S. 17th St.
1928. Houser, Karl Musser, 2035 Delancey Pl.

1938. Howell, John Carnett, 326 S. 19th St.
1948. Howland, Alvin Wilcox, 255 S. 17th St.
1946. Howson, John Yeatts, 316 Lancaster Ave., Wayne, Pa.
1951. Hubbard, John P., University of Penna., School of Medicine.
1947. Huber, John Franklin, Temple University Hospital.
1937. Hughes, Joseph, 111 N. 49th St.
1939. Hughes, P. Boland, 419 Hillbrook Rd., Bryn Mawr, Pa.
1923. Hume, John E., 900 S. 49th St.
1951. Hundley, J. Warren, 3818 Chestnut St.
1946. Hunt, William T., Jr., 1930 Chestnut St.
1921. Hunter, Robert John, 2035 Delancey Pl.
1926. Husik, David N., 331 S. 46th St.
1950. Imbriglia, Joseph E., 329 Shadeland Ave., Drexel Hill, Pa.
1935. Ingleby, Helen, Jewish Hospital, York & Tabor Rds.
1949. Ingraham, Norman R., Jr., Stenton and Whitemarsh Ave.
1951. Isard, Harold J., Mt. Sinai Hospital, 5th & Reid Sts.
1951. Israel, Harold L., 2031 Pine St.
1947. Israel, S. Leon, 2116 Spruce St.
1921. Ivy, Robert H., 1930 Chestnut St.
1917. Jackson, Chevalier, 3401 N. Broad St.
1932. Jackson, Chevalier L., Rittenhouse Plaza, 19th & Walnut Sts.
1934. Jacobs, Maurice, 1831 Delancey Place.
1947. Jaeger, Rudolph, Jefferson Hospital.
1941. Jeffers, William A., University of Pa. Hospital.
1928. John, Rutherford L., 256 S. 21st St.
1942. Johnson, Julian, 406 Conshohocken State Rd., Narberth, Pa.
1938. Johnson, Thomas A., 250 S. 18th St.
1918. Jonas, Leon, 255 S. 17th St.
1924. Jones, Harold W., 1930 Chestnut St.
1936. Kain, Thomas M., 403 Cooper St., Camden, N. J.
1948. Kaplan, Louis, 2040 Pine St.
1938. Kasper, Kelvin A., 135 S. 18th St.
1945. Katz, G. Henry, 111 N. 49th St.
1941. Kauffman, M. Luther, Medical Arts Bldg., Jenkintown, Pa.
1947. Kay, Calvin Frederick, Univ. of Pa. Hospital.
1947. Keefer, George Pfahler, 3708 Woodland Ave., Drexel Hill, Pa.
1938. Keeler, Harold R., 136 S. 16th St.
1949. Keiserman, Joseph, 5460 Baltimore Ave.
1935. Kelley, George F. J., N.E. Cor. 20th and Chestnut Sts.
1932. Kelly, Herbert T., 1900 Spruce St.
1912. Kelly, Thomas C., 105 School Lane.
1941. Kennedy, Patrick J., 6910 Market St., Upper Darby, Pa.
1947. Kennedy, William Blair, 3400 Spruce St.
1948. Kern, Franklin Moore, 537 S. 46th St.
1921. Kern, Richard A., Temple University Hospital.
1935. Keyes, Baldwin L., 2031 Locust St.
1930. Kimbrough, Robert A., Jr., 807 Spruce St.
1936. King, Orville C., 330 S. 9th St.
1920. Klauder, Joseph V., 1934 Spruce St.
1920. Klein, Thomas, 250 S. 18th St.
1934. Kline, Oram R., 514 Cooper St., Camden, N. J.
1948. Klingensmith, Paul O., 133 S. 36th St.
1932. Klopp, John W., 731 E. Phil-Ellena St.

1919. Knipe, Norman L., 1930 Chestnut St.
1908. Knowles, Frank C., 423 Warick Rd., Wynnewood, Pa.
1945. Kobler, H. B., 658 N. 63rd St.
1948. Koerber, Kenneth A., 6101 Wayne Ave.
1914. Kolmer, John A., Cynwyd, Pa.
1936. Konzelmann, Frank Williamson, 12 E. Lenox St., Chevy Chase, Md.
1949. Koop, C. Everett, 1740 Bainbridge St.
1941. Krall, J. Thomas, 1927 Spruce St.
1948. Kramer, David W., 2007 Pine St.
1944. Krauss, Frederick Harold, 2014 Delancey Place.
1949. Kremer, David N., 1918 Pine St.
1949. Kressler, Robert J., 330 S. 9th St.
1941. Krewson, William E., 3rd, 1930 Chestnut St.
1914. Krumbhaar, Edward B., School of Medicine, Univ. of Pa.
1947. Kuhlenbeck, Hartwig, Woman's Medical College.
1947. La Boccetta, Alfred Charles, 2nd and Luzerne Sts.
1949. La Clair, Charles H., Jr., 1021 W. Main St., Norristown, Pa.
1951. Lame, Edwin L., 51 N. 39th St.
1950. Lamont, Austin, 3400 Spruce St.
1946. Lampe, William T., 4207 Tyson Ave.
1933. Langdon, Roy L., 5917 Greene St.
1941. Langner, Paul H., Jr., 130 S. 18th St.
1945. Lansbury, John, 3401 N. Broad St.
1934. Laplace, Louis B., 1930 Chestnut St.
1926. Laws, George M., 1907 Spruce St.
1936. Leaman, William G., Jr., 3700 Baring St.
1950. Learner, Norman, 255 S. 17th St.
1920. Leavitt, Frederic Headley, 1527 Pine St.
1941. Leberman, Paul R., 136 S. 16th St.
1942. Lehman, James A., 255 S. 17th St.
1936. Lehrfeld, Louis, 1321 Spruce St.
1951. Leivy, Frank E., 1321 Spruce St.
1944. Lell, William A., 203 W. Chestnut Ave.
1935. Lemmon, William T., 1930 Chestnut St.
1943. Leopold, Irving H., 1930 Chestnut St.
1920. Leopold, Simon S., 255 S. 17th St.
1944. Lettiere, Anthony J., 425 E. State St., Trenton, N. J.
1933. Levering, J. Walter, Abington Memorial Hospital, Abington, Pa.
1915. Lewis, Fielding O., Providence Road, Media, Pa.
1938. Lewis, James P., 3815 Chestnut St.
1949. Lhamon, William T., Monument Road, Bala-Cynwyd, Pa.
1948. Lieber, Marshall M., 1025 Walnut St.
1948. Lieberman, Louis M., 923 Belmont Ave.
1940. Limberger, William A., 301 S. Church St., West Chester, Pa.
1938. Lindauer, M. August, 133 S. 36th St.
1927. Lindsey, Walter H., 810 W. Dauphin St.
1936. Lintgen, Charles, 1930 Chestnut St.
1945. Lisker, Samuel, 1930 Chestnut St.
1944. Livezey, Mary M., 7200 Cresheim Rd.
1936. Llewellyn, Thomas H., 910 N. 63rd St.
1907. Lodholz, Edward, 431 S. 45th St.
1931. Loewenberg, Samuel A., 1905 Spruce St.
1938. Long, Charles-Francis, 1128 70th Ave.

1933. Long, Esmond R., Henry Phipps Institute, 7th and Lombard Sts.
1949. Long, Joan Humphrey, 17B Parkway Apartments, Haddonfield, N. J.
1951. Long, Joseph P., 1930 Chestnut St.
1935. Long, William L., 2025 Walnut St.
1931. Longaker, Edwin P., 41 E. Montgomery Ave., Ardmore, Pa.
1951. Lorber, Stanley H., 3400 N. Broad St.
1936. Lucchesi, Pascal Francis, 601 E. Gorgas Lane.
1921. Lucké, Balduin H. E., School of Medicine, Univ. of Pa.
1932. Lukens, Francis D. W., Univ. of Pa. Hospital.
1930. Lukens, Robert M., 1308 W. Hunting Park Ave.
1939. Luongo, Romeo A., 2054 Locust St.
1947. Lurie, Max B., Henry Phipps Institute, 7th and Lombard St.
1951. Luscombe, Herbert A., 136 S. 16th St.
1919. Lynch, Frank B., Jr., Germantown Hosp., Penn and Chew Sts.
1950. Lynch, J. Edward, 255 S. 17th St.
1914. Lyon, B. B. Vincent, Box 955, Winter Park, Fla.
1933. McAndrews, Leo F., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1932. McCahey, James F., 1534 Pine St.
1948. McCall, Milton L., 1930 Chestnut St.
1900. McCarthy, Daniel J., 2025 Walnut St.
1936. McCarthy, Patrick A., Central Medical Bldg.
1935. McClenahan, William U., 1 Summit Ave.
1931. McCloskey, Edward, 7 E. Chestnut Ave.
1942. McCloskey, John F., 8720 Germantown Ave.
1935. McConnell, James W., 20th and Chestnut Sts.
1934. McCouch, Grayson P., Medical School, Univ. of Pa.
1938. McCrea, Lowrain E., 1930 Chestnut St.
1937. McCutcheon, Morton, Alden Park Manor.
1942. McDonald, P. Robb, 1930 Chestnut St.
1950. McFadden, William M., 1187 E. Washington Lane.
1949. McGavic, John S., 601 Montgomery Ave., Bryn Mawr, Pa.
1945. McGee, Lemuel Clyde, Hercules Powder Company, Wilmington, Del.
1937. McGuinness, Aims C., Children's Hospital, 1740 Bainbridge St.
1940. McLaughlin, Edward F., 4116 N. Broad St.
1933. McLaughlin, James S., 330 S. 9th St.
1924. McMillan, Thomas M., 2044 Locust St.
1924. McPhedran, F. Maurice, Germantown Hosp., Penn and Chew Sts.
1943. Macfarlan, Douglas, 1805 Chestnut St.
1932. Macfarlane, Catharine, 136 S. 16th St.
1947. Machella, Thomas E., 232 S. 39th St.
1950. Mackmull, Gulden, Germantown Professional Building.
1949. MacNeal, Perry Scott, 330 S. 9th St.
1939. Macneill, Norman N., 5807 Chew St.
1951. Mac Neish, W. J., Medical Arts Bldg., 16th & Walnut Sts.
1935. Maeder, LeRoy M. A., 1910 Rittenhouse Sq.
1942. Manges, Lewis C., Jr., 319 S. 16th St.
1936. Mann, Bernard, 2019 Pine St.
1948. Marden, Philip Ayer, 1912 Spruce St.
1937. Margolies, Alexander, 1351 Tabor Rd.
1950. Mark, George E., 3401 N. Broad St.
1950. Marshall, E. Wayne, Jr., 1520 Spruce St.
1941. Martin, James R., 136 S. 16th St.
1951. Martin, William L., 1737 Chestnut St.

1939. May, Hans, 255 S. 17th St.
1951. Mayock, Robert L., 133 S. 36th St.
1934. Mecray, Paul M., 405 Cooper St., Camden, N. J.
1951. Medinger, Frederick G., 7214 Lincoln Drive.
1941. Mendell, Theodore H., 2023 Spruce St.
1951. Mendelssohn, Edwin, 255 S. 17th St.
1949. Menkin, Valy, 3401 N. Broad St.
1943. Meranze, David R., 1031 Lakeside Ave.
1937. Meyer, George Phillip, 410 Haddon Ave., Camden, N. J.
1935. Miller, Ford A., 4016 Chestnut St.
1946. Miller, Franklin R., Jefferson Medical College.
1939. Miller, Malcolm W., 255 S. 17th St.
1939. Miller, Merle M., 6013 Greene St.
1932. Miller, M. Valentine, 114 W. Phil-Ellena St.
1921. Miller, T. Grier, 133 So. 36th St.
1937. Missett, Joseph Vincent, Jr., 2031 Locust St.
1904. Mitchell, Charles Franklin, 2003 Pine St.
1950. Mitchell, John McK., Medical School, Univ. of Pa.
1948. Mogavero, Francesco, 1930 Chestnut St.
1932. Mohler, Roy W., 1806 Spruce St.
1936. Montgomery, Hugh, 119 Glenn Road, Ardmore, Pa.
1936. Montgomery, John B., 1930 Chestnut St.
1932. Montgomery, Thaddeus L., 2031 Locust St.
1951. Moore, Edward J., 204 Meeting House Lane, Merion, Pa.
1935. Moore, John Royal, Beury Bldg., Broad St. and Erie Ave.
1947. Moore, Matthew Thibaud, 1813 Delancey Pl.
1924. Moorhead, Stirling W., 1523 Pine St.
1936. Morgan, David R., Jefferson Medical College.
1893. Morris, Elliston J., 439 Midland Ave., St. Davids, Del. Co., Pa.
1944. Morris, Harold H., Villa Nova, Pa.
1945. Morris, I. Paul, 255 S. 17th St.
1949. Motley, Hurley L., 901 Remington Road, Wynnewood, Pa.
1941. Mucklé, Craig Wright, 255 S. 17th St.
1929. Mudd, Stuart, Department of Bacteriology, Medical School, Univ. of Pa.
1949. Mulholland, Stanford W., 255 S. 17th St.
1935. Mullen, Carroll Richard, 2025 Locust St.
1934. Mullen, Edward A., 472 Roxborough Ave.
1930. Murphy, Douglas P., Univ. of Pa. Hospital.
1934. Murphy, Eugene C., 1841 S. Broad St.
1951. Myers, David, 304 S. 19th St.
1945. Naide, Meyer, 2034 Spruce St.
1951. Naidoff, David, 37 S. 20th St.
1950. Nardone, Anthony A., 912 S. 49th St.
1950. Neefe, John R., 2016 Delancey Pl.
1948. Neese, Paul H., 17 Derwen Road, Cynwyd, Pa.
1936. Nelson, Guy M., 255 S. 17th St.
1943. Nelson, Waldo E., 615 Moreno Rd., Narberth, Pa.
1905. Newcomet, William S., 3501 Baring St.
1938. Newton, Zachariah B., 601 E. Sedgwick St.
1935. Nicholson, Jesse Thompson, Pennsylvania Hospital.
1941. Nisbet, Verner, 254 S. 45th St.
1950. Nixon, Norman, 111 N. 49th St.
1947. Noone, Ernest L., 4501 Cedar Lane, Drexel Hill, Pa.

1905. Norris, Charles C., Darby and Goshen Roads, Bryn Mawr, Pa.
1938. Norris, Robert F., 513 Wynnewood Ave., Wynnewood, Pa.
1947. O'Keefe, John J., 255 South 17th St.
1913. O'Neal, Alexander Hay, St. Davids, Pa.
1949. O'Neill, James F., 8050 Holmes Ave.
1947. Ornsteen, A. M., 2007 Delancey Pl.
1947. Ornston, Darisu Gray, 36 Carpenter Lane.
1936. Orr, Theodore, 1930 Chestnut St.
1913. Outerbridge, George W., 1927 Spruce St.
1915. Owen, Hubley R., 311 S. Juniper St.
1949. Padis, Nicholas, 255 S. 17th St.
1909. Parish, Benjamin Dores, 1927 Spruce St.
1945. Park, Felix Roman, Medical Arts Bldg., Tulsa, Okla.
1940. Parker, Alan P., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1948. Parkhurst, Leonard Woods, 330 S. 9th St.
1944. Paschkis, Karl E., Jefferson Medical College.
1931. Paul, John Davis, 3112 N. Broad St.
1932. Payne, Franklin L., Univ. of Pa. Hospital.
1943. Pearson, Gerald H. J., 11 N. 49th St.
1930. Pendergrass, Eugene P., Univ. of Pa. Hospital.
1932. Pennell, Howard Y., West Chester, Pa.
1914. Pepper, O. H. Perry, Univ. of Pa. Hospital.
1916. Percival, Milton Fraser, 2332 S. Broad St.
1942. Perkins, William Harvey, 1025 Walnut St.
1946. Perloff, William Harry, 1930 Chestnut St.
1951. Perri, Angelo M., 814 Federal St.
1940. Pessel, Johannes, F., 224 West State St., Trenton, N. J.
1940. Pettit, Horace, Times Medical Bldg., Ardmore, Pa.
1949. Pettit, Mary DeWitt, 1930 Spruce St.
1905. Pfahler, George E., 1930 Chestnut St.
1915. Pfeiffer, Damon B., Meadowbrook, Pa.
1946. Pfeiffer, Mildred C. J., 331 S. Smedley St.
1935. Phillips, Arthur W., 3904 Walnut St.
1911. Piersol, Georog Morris, Univ. of Pa. Hospital.
1948. Pierson, Daniel B., Jr., 1830 Delancey St.
1933. Pillsbury, Donald M., Univ. of Pa. Hospital.
1950. Pincus, Irwin J., 269 S. 19th St.
1951. Poinsard, Paul J., 2031 Locust St.
1937. Polk, David Stewart, Rosemont, Pa.
1932. Porter, Roland De Lance, Jenkintown, Pa.
1951. Post, Joseph W., 1930 Chestnut St.
1951. Pote, Harry H., 4032 Walnut St., Phila. 4
1949. Pratt, Gerald E., 3009 Frankford Ave.
1951. Pressman, Robert S., 269 S. 19th St.
1947. Prickett, John A., Warrington, Bucks County, Pa.
1931. Pryor, Charles Allen, 255 S. 17th St.
1947. Putney, Floyd Johnson, 255 South 17th St.
1943. Radbill, Samuel X., 7043 Elmwood Ave.
1945. Rakoff, Abraham Edward, 269 S. 19th St.
1931. Ramsey, Frank M., 620 E. Willow Grove Ave.
1941. Rankin, Charles A., Ludlow & Heather Rd., Upper Darby, Pa.
1946. Rapoport, Milton, Children's Hospital, 1740 Bainbridge St.
1951. Rathmell, Thomas K., 446 Bellevue Ave., Trenton, N. J.

1926. Ravdin, I. S., Univ. of Pa. Hospital.
1928. Reese, Warren S., 2118 Locust St.
1925. Reeves, Rufus S., 2227 Spruce St.
1920. Reifuss, Martin E., 131 St. George's Rd., Ardmore, Pa.
1921. Reiff, E. Paul, 1927 Spruce St.
1937. Reimann, Hobart A., Jefferson Hospital.
1919. Reimann, Stanley P., 703 W. Phil-Ellena St.
1951. Rentschler, Laurence B., 5800 Ridge Ave.
1945. Rhoads, Jonathan E., Univ. of Pa. Hospital.
1936. Richards, James L., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1951. Richardson, Fred Mac D., 160 Carpenter Lane.
1919. Richardson, Russell, Methodist Episcopal Hospital.
1951. Riegel, Donald., 5110 Chester Ave.
1942. Riggs, Helena E., Philadelphia General Hospital.
1936. Ritter, Joseph A., 2405 N. 54th St.
1932. Robbins, Frederick R., 317 Milbank Rd., Bryn Mawr, Pa.
1939. Roberts, Ella, 133 S. 36th St.
1899. Roberts, Walter, 1921 Spruce St.
1932. Robertson, Harold F., 327 S. 17th St.
1903. Robertson, William Egbert, 327 S. 17th St.
1938. Roche, Philip Q., 255 S. 17th St.
1912. Rodman, John Stewart, American Board of Surgery, 255 S. 15th St.
1947. Rogers, Arthur Merriam, 133 S. 36th St.
1934. Rogers, Harry L., 1537 Pine St.
1951. Ronis, Bernard J., 2106 Spruce St.
1948. Roscoe, Constantine R., 7226 Castor Ave.
1928. Rose, Edward, 426 Owen Rd., Wynnewood, Pa.
1936. Rose, Elizabeth Kirk, 426 Owen Rd., Wynnewood, Pa.
1946. Rosemond, George Parrott, Temple University, Broad & Ontario Sts.
1948. Rothman, Maurice M., 1727 Spruce St.
1932. Rothrock, Harry A., West Chester, Pa.
1936. Rothschild, Norman, 245 S. 16th St.
1951. Rouse, George P., Jr., 2031 Locust St.
1937. Roxby, John B., P. O. Box #28, Swarthmore, Pa.
1949. Royster, Henry P., 3400 Spruce St.
1941. Royster, Hubert A., Jr., The Mermont, Bryn Mawr, Pa.
1933. Rudolphy, Jay Besson, 230 S. 21st St.
1946. Rupp, Charles, 133 S. 36th St.
1947. Rush, Alexander, 330 South 9th St.
1945. Rynes, Samuel E., 334 S. 21st St.
1944. Sampson, David Alan, 726 Braeburn Lane, Penn Valley, Narberth, Pa.
1936. Sands, Joseph Evans, Rosemont, Pa.
1950. Sarner, Joseph B., 1803 Pine St.
1949. Saul, Leon J., 255 S. 17th St.
1908. Sautter, Albert C., Germantown Professional Bldg.
1947. Sayen, John J., 506 Montgomery Ave., Haverford, Pa.
1948. Scarano, Joseph Albert, 1432 S. Broad St.
1920. Scarlett, Hunter W., 825 Montgomery Ave., Bryn Mawr, Pa.
1917. Schaeffer, J. Parsons, Daniel Baugh Institute, 307 S. 11th St.
1929. Scheffey, Lewis C., 255 S. 17th St.
1942. Scheie, Harold G., 313 S. 17th St.
1929. Schenck, Harry P., 1235 Wyngate Rd., Wynnewood, Pa.
1945. Schlezinger, Nathan S., 255 S. 17th St.

1917. Schnabel, Truman G., 1704 Pine St.
1917. Schoff, Charles H., Media, Pa.
1928. Schofield, Frederick S., 8328 Germantown Ave.
1921. Schumann, Edward A., 1814 Spruce St.
1950. Schumann, Francis N., 8811 Germantown Ave.
1948. Schwarz, Gabriel A., 255 S. 17th St.
1930. Scott, John Porter, Children's Hospital, 1740 Bainbridge St.
1950. Scott, Michael, 255 S. 17th St.
1940. Scott, T. F. McNair, Children's Hospital, 1740 Bainbridge St.
1951. Seitchik, Joseph N., 1417 Race St., Hahnemann Medical College Annex.
1951. Shaffer, Bertram, 1825 Pine St.
1924. Shallow, Thomas A., 1611 Spruce St.
1950. Sharp, Reuben L., 719 Cooper St., Camden, N. J.
1928. Sharpless, Frederick C., Rosemont, Pa.
1948. Shay, Harry, 255 S. 17th St.
1946. Shepherd, Samuel Garfield, 2039 Pine St.
1932. Sheridan, Joyce T., 412 W. Durham St.
1936. Shipman, James Shelby, 255 S. 17th St.
1935. Shoemaker, Robert, 3rd, 68 Byberry Rd., Hatboro, Pa.
1951. Shorey, Winston K., 133 S. 36th St.
1946. Shoup, George Daniel, 7007 N. 12th St.
1936. Shuster, Benjamin H., 1824 Pine St.
1949. Sidlick, David M., 255 S. 17th St.
1941. Silcox, Louis E., 255 S. 17th St.
1907. Sinkler, Francis W., 514 N. Rose Lane, Bryn Mawr, Pa.
1933. Smelzer, Donald Campbell, 311 S. Juniper St.
1929. Smith, Austin T., 1830 Spruce St.
1947. Smith, Frederick C., 409 S. 22nd St.
1933. Smith, Lauren Howe, 111 N. 49th St.
1927. Smyth, Calvin Mason, Abington Memorial Hospital, Abington, Pa.
1951. Snape, William J., 573 Stevens St., Camden, N. J.
1938. Snodgrass, L. E., 2011 Chestnut St.
1935. Sokoloff, Martin J., 255 S. 17th St.
1940. Soloff, Louis A., 255 S. 17th St.
1950. Somerville, William J., 2022 Locust St.
1935. Sommer, George N. J., 120 W. State St., Trenton, N. J.
1944. Sommer, George N. J., Jr., 120 W. State St., Trenton, N. J.
1951. Sonneborn, Duane G., 1200 W. Erie Ave.
1928. Spaeth, Edmund B., 1930 Chestnut St.
1937. Spangler, John Luther, Devon, Pa.
1935. Spiegel, Ernest, 6807 Lawnton Ave., Oa, Lane.
1944. Stadie, William C., University Hospital.
1927. Starr, Isaac, 505 Cresheim Valley Rd.
1945. Stecher, H. Armin, 1510 Darby Rd., Havertown, Pa.
1946. Stein, Irvin, 1936 Spruce St.
1947. Steiner, Charles A., Upper Darby, National Bank Building, Upper Darby, Pa.
1936. Steinfield, Edward, N. E. Cor. 18th and Chestnut Sts.
1942. Stengel, Alfred, Jr., Lancaster Ave. and Cambria Court, St. Davids, Pa.
1951. Sterling, Julian A., 255 So. 17th St.
1948. Stevens, Lloyd W., 133 S. 36th St.
1941. Stewart, Winifred B., 1930 Spruce St.
1949. Stockwell, Eunice L., 2018 Pine St.
1925. Stokes, John H., 4228 Spruce St.

1928. Stokes, Joseph, Jr., Children's Hospital, 1740 Bainbridge St.
1943. Stokes, S. Emlen, 129 Chester Ave., Moorestown, N. J.
1923. Strecker, Edward A., 111 N. 49th St.
1923. Stroud, William Daniel, 1011 Clinton St.
1937. Strumia, Max M., Penn Valley, Narberth, Pa.
1933. Stuckert, Harry, 248 S. 21st St.
1937. Sturgis, Margaret C., 349 Wistar Rd., Wynnewood, Pa.
1927. Sturgis, Samuel Booth, 349 Wistar Rd., Wynnewood, Pa.
1934. Summey, Thomas J., 330 S. 9th St.
1930. Sunderman, F. William, 6627 Greene St.
1936. Surver, James Miller, 1020 Clinton St.
1928. Swartley, William B., 6002 Greene St.
1944. Swenson, Paul C., Jefferson Hospital.
1948. Tait, Edwin Forbes, 1324 Main St., Norristown, Pa.
1943. Tassman, Isaac S., 136 S. 16th St.
1948. Tatnall, Charles R., Times Medical Building, Ardmore, Pa.
1946. Tauber, Robert, 2019 Walnut St.
1933. Taylor, Herbert W., Haverford, Pa.
1931. Taylor, Norman H., 100 W. Evergreen Av.
1951. Theodos, Peter A., 1930 Chestnut St.
1946. Thomas, Carmen C., 1930 Chestnut St.
1928. Thomas, J. Earl, Drexel Hill, Pa.
1927. Thorington, J. Monroe, 2031 Chestnut St.
1936. Thornton, Mary Bickings-, 2703 West Somerset St.
1936. Thorp, Francis Quicksall, 4900 Penn St.
1936. Thudium, William J., 136 S. 16th St.
1935. Tocantins, Leandro Maués, 424 W. Hortter St.
1945. Toland, Joseph J., Jr., 1241 W. Lehigh Ave.
1935. Toland, Owen J., Episcopal Hospital, Front and Lehigh Ave.
1949. Tornay, Anthony S., 37 S. 20th St.
1945. Tourish, William J., 1115 Childs Ave., Drexel Hill, Pa.
1949. Town, Arno E., 255 S. 17th St.
1936. Towson, Charles Emory, Germantown Professional Bldg.
1908. Tracy, Stephen E., Old Arch Rd., Norristown, Pa.
1947. Trueman, Robert H., 1930 Chestnut St.
1926. Tucker, Gabriel, 250 S. 18th St.
1938. Tuft, Louis, 1530 Locust St.
1933. Tumen, Henry J., 1900 Rittenhouse Sq.
1938. Turman, Christopher M., Wyncote, Pa.
1923. Turner, Creighton H., 1731 Pine St.
1945. Twyeffort, Louis H., 111 N. 49th St.
1929. Tyson, Ralph M., 255 S. 17th St.
1937. Uhle, Charles A. W., 255 S. 17th St.
1950. Ullery, John C., 255 S. 17th St.
1907. Ullom, Josephus T., Carpenter and Quincy Sts.
1950. Valdes-Dapena, Antonio, 101 Washington Ave., Havertown, Pa.
1937. Vander Veer, Joseph B., 330 S. 9th St.
1937. Van Loon, Emily Lois, 1930 Chestnut St.
1933. Vastine, Jacob H., 2nd, 136 S. 16th St.
1947. Vastine, Mary F., Woman's Medical College of Pa.
1940. Voegelin, Adrian W., Germantown Professional Bldg.
1941. Vogel, Stoughton R., 246 Walnut Lane.
1903. Wadsworth, William S., 4632 Hazel Ave.

1927. Wagers, Arthur J., 1429 Spruce St.
1949. Wagner, Frederick B., Jr., 251 S. 41st St.
1949. Wagner, Joseph A., 2720 Darby Rd., Havertown, Pa.
1928. Wagoner, George W., Haverford Gables, Haverford, Pa.
1938. Waldman, Joseph, 404 Meadowbrook Lane.
1906. Walker, John K., 139 Little Lane, Haverford, Pa.
1907. Walker, Warren, 511 Lynmere Rd., Bryn Mawr, Pa.
1932. Walkling, Adolph A., 136 S. 16th St.
1932. Watt, Charles C., Jr., 100 W. Coulter St.
1933. Waygood, James Jamison, 3464 School Lane.
1941. Weaver, Ruth H., 2601 Parkway.
1930. Weeder, S. Dana, 250 W. Tulpehocken St.
1920. Weidman, Fred D., 20 Tenby Rd., Havertown, Pa.
1933. Weiss, Benjamin P., The Lenox, 13th and Spruce Sts.
1923. Weiss, Edward, 269 S. 19th St.
1950. Weiss, Sidney, 1930 Chestnut St.
1951. Welty, Jack W., Montgomery Ave. & Owen Rd., Wynnewood, Pa.
1935. Whelan, G. L., 2100 Walnut St.
1921. Whitaker, William, 4645 Oakland St.
1936. White, Ellen Pawling Corson-, 2310 Locust St.
1925. Widmann, Bernard P., 250 S. 18th St.
1936. Wilder, Theodore S., 6013 Greene St.
1935. Willard, John Harrington, 334 S. 15th St.
1939. Willauer, George, 6129 Greene St.
1907. Williams, Carl, School Lane and Greene St.
1937. Williams, John C., 6370 Germantown Ave.
1920. Williams, Philip F., 2206 Locust St.
1950. Williams, R. G., Medical School, Univ. of Pa.
1927. Williamson, Ernest G., 6353 Woodbine Ave.
1949. Willson, J. Robert, 3401 N. Broad St.
1921. Wilson, George, 133 S. 36th St.
1945. Wilson, John F., 1930 Chestnut St.
1942. Wilson, Lucius R., 1305 Morris Road, Wynnewood, Pa.
1937. Wilson, Ross B., 1820 S. Rittenhouse Sq.
1949. Wilson, William W., 133 S. 36th St.
1948. Winkelman, Nathaniel W., 1911 Spruce St.
1948. Winston, Julius, 5839 Chester Ave.
1941. Wirts, C. Wilmer, 2017 Delancey St.
1904. Wister, James W., 5430 Germantown Ave.
1933. Wohl, Michael G., 1727 Pine St.
1944. Wolf, Lewis R., 3474 Frankford Ave.
1918. Wolferth, Charles C., S.E. Cor. 36th & Spruce Sts.
1942. Wolman, Irving J., Lakeside Apts.
1893. Wood, Alfred C., 2035 Walnut St.
1950. Wood, Dorothy D., 2035 Walnut St.
1932. Wood, Francis C., 212 Laurel Lane, Haverford, Pa.
1900. Wood, George B., 329 Hathaway La., Wynnewood, Pa.
1903. Wood, Horatio C., Jr., 319 S. 41st St.
1944. Wood, H. Curtis, Jr., Skippack Pk., Whitemarsh, Pa.
1897. Woodward, George, W., Willow Grove Ave.
1928. Wright, Carroll S., 1402 Spruce St.
1937. Yaskin, Joseph C., 1832 Spruce St.
1943. Yawger, Nathaniel S., Exeter Rd., Haverford, Pa.

1921. Ylvisaker, Lauritz S., P. O. Box 268, Bryn Mawr, Pa.
1941. Young, Barton R., Germantown Hospital.
1946. Zeigerman, Joseph H., 1836 Delancey St.
1894. Zentmayer, William, 265 Forrest Rd., Merion, Pa.
1947. Zintel, Harold A., Univ. of Pa. Hospital.
1949. Zintl, William J., 1930 Chestnut St.
1933. Zulick, J. Donald, Abington Memorial Hospital, Abington, Pa.

Associate Fellows

ELECTED

1951. Shorey, Jeanette McC., University Hospital, 36th & Spruce Sts.

Non-Resident Fellows

ELECTED

1912. Addison, William H. F., 286 East Sidney Avenue, Mt. Vernon, N. Y.
1941. Aronson, Roland S., Medical Laboratory, Ft. McPherson, Ga.
1934. Bank, Joseph, 800 N. First Ave., Phoenix, Arizona.
1932. Behney, Charles A., 4030-C Urban St., Los Alamos, N. M.
1949. Bixby, Edward W., 61 W. Ross St., Wilkes-Barre, Pa.
1937. Braceland, Francis J., Mayo Clinic, 102–11 Second Ave., S.W., Rochester, Minn.
1948. Brogan, Edmond J., 129 Summit Ave., Summit, N. J.
1948 *Brown, Robert B., U. S. Naval Hospital, Bethesda, Md.
1908. Cadbury, William W., 274 W. Main St., Moorestown, N. J.
1936. Camero, Anthony R., 657 S. Westlake Ave., Los Angeles, Cal.
1941. Cheleden, John, 1206 E. Ocklawaha Ave., Ocala, Florida
1930. Clarke, Francis Mann, 116 New St., New Brunswick, N. J.
1930. Cottrell, James E., Kennedy Veteran's Administration Hospital, Memphis, Tennessee.
1940. Crowe, Aldrich C., 735 Atlantic Ave., Ocean City, N. J.
1947. Cutler, Norman L., 1300 Harrison St., Wilmington, Del.
1941. *Cuttle, Tracy D., U. S. Navy, San Leandro, California
1941. Dixon, Harold M., 2125 5th Ave., San Diego, Calif.
1897. Dorland, W. A. Newman, Route 2, Box 775, Tampa, Fla.
1951. Ervin, Carl E., 240 North Third Street, Harrisburg, Pa.
1944. Estes, W. L. Jr., Bethlehem, Pa.
1940. Forrester, James S., Harrisburg Polyclinic Hospital, Harrisburg, Pa.
1946. Forster, Francis M., Georgetown University Hospital, Washington, D. C.
1933. Fowler, Kenneth, 2535 Horton Ave., San Diego, Cal.
1947. Gaskill, Herbert S., 4528 College Ave., Indianapolis 5, Ind.
1913. Gates, Nathaniel, 10 Peterboro, Detroit, Mich.
1931. Gilman, Robert Louis, Cheyney, Pa.
1947. Grady, Hugh G., Armed Forces Institute, Washington, D. C.
1936. Guthrie, Donald, 118 S. Wilbur Ave., Sayre, Pa.
1902. Gwyn, Norman B., 109 Madison Ave., Toronto, Canada.
1936. Hatch, Lerleen Clement, 2184 Ayers Ave., Akron, Ohio.
1928. Hayman, Joseph Marchant, Jr., Lakeside Hosp., 2065 Adelbert Rd., Cleveland, Ohio.
1933. Hitzrot, Lewis H., Medical Director, Mercersburg Academy, Mercersburg, Pa.
1936. Hughes, Brady A., 312 Euclid Ave., Mt. Brook, Birmingham, Ala.
1899. Jopson, John H., Rutherfordton, N. C.
1947. Kelchner, Clyde H., 1125 Turner St., Allentown, Pa.

1931. Kinney, Willard H., 7300 Atlantic Ave., Ventnor, N. J.
1942. Kneedler, William H., 609 N. Statesville Rd., Davidson, N. C.
1944. LaMotte, William O., Medical Arts Building, Wilmington, Del.
1948. Livingood, Clarence S., School of Medicine, Univ. of Texas, Galveston, Texas.
1948. McLaughlin, John T., 1252 S. Central Ave., Glendale, Calif.
1900. McReynolds, Robert Phillips, 213 S. Broadway, Los Angeles, Cal.
1949. Manlove, Francis R., 535 N. Dearborn St., Chicago, Ill.
1935. Mason, James B., 4677 So. 34 St., Arlington, Va.
1935. Matthews, Robert A., 1542 Tulane Ave., New Orleans, La.
1932. Meade, Richard H., Jr., 750 San Jose Dr., Grand Rapids, Mich.
1936. Middleton, William Shainline, 2114 Adams St., Madison, Wisconsin.
1928. Moon, Virgil H., Univ. of Miami, Coral Gables, Fla.
1937. Nicholson, Samuel T., 2d., 642 High St., Pottstown, Pa.
1905. Norris, George W., Dimock, Pa.
1926. Paul, John Rodman, Dept. Internal Medicine, Yale University, New Haven, Conn.
1947. Pearce, Louise, Trevenna Farms, Belle Mead, N. J.
1922. Pleasants, Henry, West Chester, Pa.
1938. Read, Hilton S., 5407 Atlantic Ave., Atlantic City, N. J.
1936. Reisinger, John A., 901 20th St., N.W., Washington, D. C.
1907. Royer, B. Franklin, 429 E. Baltimore St., Greencastle, Pa.
1945. Schell, James F., Veterans Hospital, New Castle, Del.
1913. de Schweinitz, George L., 85 E. Broad St., Bethlehem, Pa.
1941. Shands, Alfred R., Jr., Alfred I. duPont Institute, Rockland Rd., Wilmington, Del.
1908. Shannon, Charles E. G., 9 Park St., Waterville, Maine
1943. Shewbrooks, Daniel N., The Acacia Mutual Life Ins. Co., Washington, D. C.
1950. Shiffer, Paul H., 111 N. 7th St., Stroudsburg, Pa.
1932. Siegel, Alvin Erdreich, Medical Arts Building, Macon, Ga.
1929. Sponsler, Marshall B., 103 Lansdowne Road, DeWitt, N. Y.
1934. Stewart, Sloan G., Pacific and North Carolina Avenues, Atlantic City, N. J.
1931. Stiles, Merritt H., 820 S. McClellan St., Spokane, Wash.
1942. Thompson, Wesley D., 18 N. Main St., Lewistown, Pa.
1941. Tompkins, Pendleton, 450 Sutter St., San Francisco, California.
1913. Vail, William Penn, Blairstown, N. J.
1912. Vaux, Norris W., Department of Health, Harrisburg, Pa.
1897. Veasey, Clarence Archibald, W. 1118–9th Ave., Spokane, Washington.
1931. Walker, Herschel Carey, 320 Park Ave., New York City, N. Y.
1914. Willard, De Forrest P., Sea Island, Ga.

Honorary Fellows

Limited to Fifty, of Whom Twenty May be Foreigners

American

ELECTED

1949. Alexander, John, Univ. of Michigan Hospital, Ann Arbor, Mich.
1947. Longcope, Warfield Theobald, Johns Hopkins Hospital, Baltimore, Md.
1917. Miner, Charles Howard, B.S., M.D., Member of Board of Directors, Wilkes-Barre General Hospital; Board of Health, Wilkes-Barre; Board of Directors, White Haven Sanitarium Association and Penna. Tuberculosis Society. 264 S. Franklin St., Wilkes-Barre, Pa.
1936. Richards, Alfred Newton, Ph.D., Sc.D., M.D. (hon.), LL.D., Professor of Pharmacology, School of Medicine, Vice-president in charge of Medical Affairs, Univ. of Pa. School of Medicine, Univ. of Pa., Phila.

1942. Russell, Frederick Fuller, M.D., Brig. Gen. Med. Corps, U. S. A. (Ret.). 4938 Brownsboro Road, Louisville, Kentucky.

1947. Stone, Robert Spencer, Univ. of California Medical School, San Francisco, Calif.

Foreign

1937. Dale, Sir Henry Hallett, C.B.E., F.R.S., M.A., M.D., F.R.C.P., Director, National Institute for Medical Research. The Wellcome Trust, 28 Portman Sq., London, W. C. England.

1922. McCarrison, Sir Robert, K.T., C.I.E., M.D., D.SC., LL.D., F.R.C.P., Major-General, Indian Medical Service (retired). 18 Linton Rd., Oxford, England.

Honorary Associates

1942. Conklin, Professor Edwin G., Princeton University, Princeton, N. J.

1942. Donner, William Henry, Fidelity-Philadelphia Trust Bldg., Philadelphia, Pa.

Necrological List

Resident Fellows	*Date of Election*	*Date of Death*
Brooke M. Anspach	December 6, 1905	July 8, 1951
Percy L. Balentine	January 5, 1916	December 11, 1951
Joseph C. Birdsall	October 3, 1917	June 30, 1951
Carl J. Bucher	January 6, 1930	October 9, 1951
Verne G. Burden	January 9, 1928	June 23, 1951
Charles D. Hart	April 1, 1903	February 14, 1951
Harriet L. Hartley	October 1, 1941	October 18, 1951
Charles J. Hatfield	March 6, 1907	August 25, 1951
Walter E. Lee	June 3, 1908	April 5, 1951
Clifford B. Lull	January 7, 1929	July 6, 1951
John F. McCloskey	May 6, 1942	November 22, 1951
William R. Nicholson	April 5, 1899	February 18, 1951
Wilbur W. Oaks	April 2, 1947	December 19, 1950
Alexander Randall	October 1, 1913	November 18, 1951
William C. Sheehan	May 11, 1931	April 12, 1951
John A. Sweeney	January 8, 1934	February 14, 1951
Samuel M. Wilson	January 5, 1902	August 12, 1951
Oscar T. Wood	April 2, 1947	August 4, 1951
Non-Resident Fellows		
George E. Price	November 6, 1907	April 24, 1951
Ralph L. Shanno	April 19, 1949	February 14, 1951

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1951

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